COMPARISON OF INTRAVENOUS INFUSION OF LIGNOCAINE VERSUS DEXMEDETOMIDINE FOR POSTOPERATIVE PAIN RELIEF IN PATIENTS UNDERGOING TOTAL LAPAROSCOPIC HYSTERECTOMY

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Submitted By

DR. VASUNDHARA JINDAL

DEPARTMENT OF ANAESTHESIOLOGY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA, PUNJAB

DECLARATION BY THE CANDIDATE

I hereby declare that the thesis entitled "**COMPARISON OF INTRAVENOUS INFUSION OF LIGNOCAINE VERSUS DEXMEDETOMIDINE FOR POSTOPERATIVE PAIN RELIEF IN PATIENTS UNDERGOING TOTAL LAPAROSCOPIC HYSTERECTOMY**" submitted towards partial fulfillment of the requirements for the award of **MD in Anaesthesiology** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr Sandeep Kundra**, Professor, Department of Anaesthesiology, **Dr. Anju Grewal**, Professor & Head, Department of Anaesthesiology and **Dr. Ashima Teneja**, Professor & Head, Department of Obstetrics and Gynaecology. No part of this thesis has formed the basis for the award of any degree previously.

_____

Dr. Vasundhara Jindal
Department of Anaesthesiology,
Dayanand Medical College & Hospital,
Ludhiana, Punjab

Date:

Place:

CERTIFICATE OF SUPERVISORS

This is to certify that the work incorporated in this thesis entitled "**COMPARISON OF INTRAVENOUS INFUSION OF LIGNOCAINE VERSUS DEXMEDETOMIDINE FOR POSTOPERATIVE PAIN RELIEF IN PATIENTS UNDERGOING TOTAL LAPAROSCOPIC HYSTERECTOMY"** has been carried out by **Dr. Vasundhara Jindal** under our direct supervision. The data incorporated in this thesis is original and genuine and has been carried out by the candidate herself.

Signature of Supervisor

Dr. Sandeep Kundra
Professor
Department of Anaesthesiology
DMC&H, Ludhiana

Signature of Co-Supervisors

Dr. Anju Grewal
Professor & Head
Department of Anaesthesiology
DMC&H, Ludhiana

Dr. Ashima Taneja
Professor & Head
Department of Obst & Gynae
DMC&H, Ludhiana

Date:

ENDORSEMENT BY THE HEAD OF THE INSTITUTE

This is to certify that the thesis entitled "**COMPARISON OF INTRAVENOUS INFUSION OF LIGNOCAINE VERSUS DEXMEDETOMIDINE FOR POSTOPERATIVE PAIN RELIEF IN PATIENTS UNDERGOING TOTAL LAPAROSCOPIC HYSTERECTOMY"** is a bonafide research work done by **Dr. Vasundhara Jindal** under the supervision of **Dr Sandeep Kundra**, Professor, Department of Anaesthesiology, **Dr. Anju Grewal**, Professor & Head, Department of Anaesthesiology and **Dr. Ashima Teneja**, Professor & Head, Department of Obstetrics and Gynaecology in this institution.

Principal

Dr. Sandeep Puri
Principal
DMC&H, Ludhiana

Date:

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Signature

Dr Vasundhara Jindal
Department of Anaesthesiology,
Dayanand Medical College & Hospital,
Ludhiana, Punjab - 141001

Date:

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Dedicated

to

my Family

&

Teachers

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Dr. Vasundhara Jindal

ABBREVIATIONS

%	Percentage
DBP	Diastolic blood pressure
ECG	Electrocardiogram
$EtCO_2$	End tidal carbon dioxide
HR	Heart rate
IV	Intravenous
Kg	Kilogram
Kg/m^2	$Kilogram/meter^2$
m^2	$meter^2$
MAP	Mean arterial pressure
Mg	Milligram
Mg/hr	Milligram/hour
Mg/kg	Milligram/kilogram
Mm Hg	Millimeter of mercury
N_2O	Nitrous oxide
NIBP	Non-invasive blood pressure
NSAIDS	Non steroidal anti inflammatory drugs
O_2	Oxygen
RR	Respiratory rate
SBP	Systolic blood pressure

DBP	Diastolic blood pressure
SpO_2	Oxygen saturation
t ½	Half life
VAS	Visual Analogue Scale
Inj.	Injection
Mcg/kg/hr	Microgram/kilogram/hour
Mg/kg/hr	Milligram/kilogram/hour
TLH	Total laparoscopic hysterectomy
PACU	Post anaesthesia care unit
Hr	Hours
NRS	Numerical Rating Scale
IL-1	Interleukin-1
IL-6	Interleukin-6
TNF	Tumor necrosis factor

ABSTRACT

Introduction: A major concern after surgery is postoperative pain. Opioids, used for postoperative pain, cause nausea and constipation. Therefore, non-opioid modalities are being investigated to control postoperative pain, thus preventing over-reliance on opioids.

Aims and objectives: To compare the efficacy of perioperative intravenous lignocaine and intravenous dexmedetomidine on postoperative pain management after total laparoscopic hysterectomy.

Methods Sixty patients posted for total laparoscopic hysterectomy were randomized into two groups. Group A patients received 1.5 mg/kg bolus dose of intravenous lignocaine before induction, followed by 1 mg/kg/hr infusion, while Group B patients received 1 µg/kg bolus dose of dexmedetomidine before induction followed by a 0.6 µg/kg/hr infusion, with both infusions continued for 24 hours postoperatively. Postoperative visual analog scale (VAS) and opioid consumption, hemodynamic parameters, time of administration, and number of times rescue analgesia administered, adverse effects were recorded.

Results: The mean VAS score and total opioid consumption were comparable in both the groups at all time measurement intervals. The time to first and second rescue analgesia administration was significantly longer in group B than group A. The mean heart rate was comparable in both the groups till 3 hours, thereafter till 24 hours, mean HR was significantly lower in the group B than group A. The mean SBP values in the postoperative period were similar in both the groups till 1st hour. Thereafter, till 24 hours, the mean SBP was significantly lower in group B than group A. The mean oxygen saturation and mean respiratory rate in both the groups was comparable at all time intervals. The incidence of adverse effects like bradycardia and hypotension was higher in group B than Group A.

Conclusion: Both lignocaine and dexmedetomidine are equi-efficacious in reducing postoperative pain after total laparoscopic hysterectomy. However dexmedetomidine is associated with a higher incidence of adverse effects like bradycardia and hypotension, therefore necessitating rigorous and vigilant monitoring in this group of patients.

Keywords: Lignocaine, dexmedetomidine, postoperative pain, total laparoscopic hysterectomy

TABLE OF CONTENTS

S. NO.	TOPIC	PAGES
I	INTRODUCTION	1-5
II	AIMS AND OBJECTIVES	6
III	REVIEW OF LITERATURE	7-21
IV	MATERIALS AND METHODS	22-27
V	OBSERVATIONS AND RESULTS	28-57
VI	DISCUSSION	58-68
VII	SUMMARY AND CONCLUSIONS	69-71
VIII	BIBLIOGRAPHY	72-82
	APPENDICES – I - PROFORMA - MASTER CHART	
	APPENDICES – II - APPROVAL LETTER OF THESIS PLAN - THESIS PLAN	

LIST OF TABLES

Table No.	Title	Page No.
1.	Mean age distribution (years)	29
2.	Mean height (cm)	30
3.	Mean weight (kg)	31
4.	Mean BMI (kg/m^2)	32
5.	ASA physical status	33
6.	Trends in the postoperative mean heart rate (per minute)	34
7.	Trends in the postoperative mean systolic blood pressure (mm Hg)	36
8.	Trends in the postoperative mean diastolic blood pressure (mmHg)	38
9.	Trends in the Postoperative SpO2 (%)	40
10.	Trends in postoperative mean respiratory rate (breaths per minute)	42
11.	Trends in postoperative mean VAS score at rest at various time intervals	44
12.	The mean VAS score at time of administration of each rescue analgesic	46
13.	Mean time to first rescue analgesic consumption (minutes)	47
14.	Mean time to second rescue analgesic consumption (minutes)	48
15.	Total rescue analgesic (tramadol) consumption in 24 hours (mg)	49
16.	Number of times rescue analgesia given	50
17.	Mean Ramsay sedation score	51
18.	Incidence of postoperative adverse effects (%)	52
19.	Mean atropine bolus administered	54
20.	Mean ephedrine bolus administered	56

LIST OF FIGURES

Fig. No.	Title	Page No.
A	Visual analogue scale	25
1.	Mean age distribution (years)	29
2.	Mean height (cm)	30
3	Mean weight (kg)	31
4	Mean BMI (kg/m^2)	32
5	ASA physical status	33
6.	Trends in the postoperative mean heart rate (per minute)	35
7.	Trends in the postoperative mean systolic blood pressure (mm Hg)	37
8.	Trends in the postoperative mean diastolic blood pressure (mmHg)	39
9.	Trends in the Postoperative SpO2 (%)	41
10.	Trends in postoperative mean respiratory rate (breaths per minute)	43
11.	Trends in postoperative mean VAS score at rest at various time intervals	45
12.	The mean VAS score at time of administration of each rescue analgesic	46
13.	Mean time to first rescue analgesic consumption (minutes)	47
14.	Mean time to second rescue analgesic consumption (minutes)	48
15.	Total rescue analgesic (tramadol) consumption in 24 hours (mg)	49
16.	Number of times rescue analgesia given	50
17.	Mean Ramsay sedation score	51
18.	Incidence of postoperative adverse effects (%)	53
19.	Mean atropine bolus administered	55
20.	Mean ephedrine bolus administered	57

INTRODUCTION

Ever since total laparoscopic hysterectomy first came into clinical practice in benign gynecology, there has been evidence to suggest its benefits over total abdominal hysterectomy and vaginal hysterectomy.[1] The main advantages are reduced postoperative pain, quicker postoperative recovery, lower rates of early and late postoperative complications, and earlier mobilization.[2] Hospital stay is also shorter than even vaginal hysterectomy.[1] Though pain after laparoscopic hysterectomy is less compared to open hysterectomy, still most patients complain of mild to moderate intensities of pain, which if untreated, can result in chronic pain. Therefore, postoperative pain needs to be managed optimally not only to provide rapid recovery but also to prevent long-term consequences like chronic pain. [3,4]

The definition of pain has been revised by the International Association for Study of Pain as “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage”.[5] After laparoscopic surgery, numerous factors are responsible for pain such as injury to nerves, vessels, and abdominal wall, a surge in inflammatory cytokines production, pneumo-peritoneum consequent to insufflation of carbon dioxide, excitation of the phrenic nerve, elevated intra-abdominal pressures in the course of surgery, as well as intraoperative visceral dissection.[6,7] Pain arises from port incision sites within the abdominal wall, pneumo-peritoneum, lower abdominal pain from intraperitoneal manipulations, and tissue dissection within the pelvis.[6,7] Two types of pain can be experienced after laparoscopic surgery - somatic pain and visceral pain.[8] Somatic pain is due to incision to skin, muscles, and ligaments while visceral pain is due to manipulation of internal organs.[9] Pain from visceral dissection is relatively more than incisional pain. Shoulder pain also stays intense in 90% of patients and may continue up to 72 hours after surgery with a maximum intensity at 24 hours in the postoperative period. The most common sites of pain include

port wounds, shoulder tip, region of flanks, lower abdomen, and perineum during the first 24 hours, with perineum pain being more severe than abdominal pain in one-third of patients.[7] Upper abdominal, and postural high back pain have also been documented after laparoscopic hysterectomy.[10]

Various other factors determine the post laparoscopy pain- residual gas volume, the temperature of the insufflated gas, and the rate at which gas has been insufflated.[11,12] The nature and technique of surgery, the anesthetic, and analgesic interventions also determine postoperative pain intensity.[13] Inadequately managed pain significantly extends recovery time and is linked to an increase in morbidity, quality and functional impairment of life, escalation of health care expenditure, the prolonged period of use of opioids, and pain that becomes chronic or persistent.[13]

To treat this post laparoscopy acute pain, an 'ideal analgesic' must be tolerated well, have a rapid onset of action, and produce analgesia over a wide range of pain types in different patient populations.[14] In search of an ideal analgesic for reducing pain postoperatively, many studies have been conducted using a variety of methods- preoperative administration of anti-inflammatory drugs, the combination of non-steroidal anti-inflammatory drugs and opioids, intravenous infusions of local anesthetics and alpha agonists, utilizing carbon dioxide at body temperature, intraperitoneal instillation, and surgical wound infiltration with local anesthetics.[15] However, a single analgesic regimen has not been successful in optimally managing pain without major strains on equipment, surveillance systems, or significant side effects. The intensity of pain and hence the selection of analgesics also depends upon the expertise of surgeons and anesthetists, the duration of surgery and the social, genetic, and racial differences of patients.[10] Therefore, the key principles for a good postoperative recovery are having a multimodal regimen and regular pain scoring, and encouraging patients to ask for analgesia.[10]

The multimodal analgesia technique is a popular technique to manage postoperative pain. It includes combining medications that have additive or synergistic effects and different mechanisms of action, to augment the potency of individual drugs while minimizing their secondary adverse effects.[16] Commonly combined medication groups are local anesthetics, opioids, non-steroidal anti-inflammatory drugs, acetaminophen, and alpha-2 agonists.[17]

Another concept in managing postoperative pain is preemptive analgesia. Before the surgical stimulus, analgesic drugs are administered. This gives more time for better drug absorption and distribution to the target site by the time the patient wakes up after general anesthesia. Pain intensity is thus decreased as compared to cases where analgesia has been given after the surgical stimulus. [10]

Opioids have always been an important component of analgesic regimens but their associated complications- sedation, respiratory depression, nausea, ileus have prompted researchers to suggest a restriction in their usage.[16] Drugs such as intravenous paracetamol, intravenous diclofenac, cyclooxygenase- 2 inhibitors in combination with opioids do not necessarily meet all the requirements of post-surgical patients, without causing significant side effects.[10] Regional analgesia and central neuraxial analgesia with local anesthetics, do inhibit catabolic stress response and improve cardiopulmonary function, but administration of regional analgesia requires a highly skilled practitioner to avoid potential complications.[17] Also, the issue of postoperative ileus remains unresolved.[16] Therefore, additional options to provide non-opioid analgesia and enable a rapid recovery are desirable.

The most efficacious route of administration of postoperative analgesia is also under study. Oral analgesics can be given but only after the patient can tolerate drinking. Also in case of postoperative nausea and vomiting, this might not be a suitable route. Regional blocks can be given but they are associated with neurological risks and have no effect on postoperative

ileus.[10] The intramuscular route can also be employed but after surgery, hypovolemia and hypothermia can affect analgesic absorption leading to inadequate analgesia. The intravenous route is the fastest route of administration of analgesics. Patients will often have an intravenous cannula in place for several hours after surgery, and therefore the intravenous route is one of the best possible routes of postoperative analgesia, especially in the presence of postoperative nausea and vomiting.[10]

In search of effective non-opioid analgesics, intravenous lignocaine and dexmedetomidine have been studied. Intravenous lidocaine has peripherally and centrally mediated analgesic, anti-inflammatory, and anti-hyperalgesic properties. At plasma concentration levels of 0.5-5 mcg/ml, lignocaine is observed to have analgesic benefits, when given as an intravenous infusion. It induces global analgesia and dampens the neuro-inflammatory response in pain. Lignocaine has a large therapeutic window and is easy to use. It also improves wound healing, postoperative cognitive dysfunction, and ileus. In addition, its large safety profile allows less analgesic use and early recovery from anesthesia, making it one of the best additives in the multimodal approach to postoperative pain control.[18]

Dexmedetomidine is an alpha2-adrenoreceptor agonist and possesses analgesic properties due to a reduction in sympathetic tone. It also has sedative and anxiolytic potential, and attenuation of the stress response with no significant respiratory depression. Sedation is reversible and resembles a more natural sleep-like state, except at doses that cause deep sedation or general anesthesia. However, dexmedetomidine also has potential adverse effects such as hypotension and bradycardia that must be taken into consideration when administered. Therefore, clinical trials are needed to establish safe optimal doses that provide the maximum benefit with minimum side effects.[19]

Multimodal analgesia is recommended during the total laparoscopic hysterectomy for reducing postoperative pain, but the medical literature does not have definite conclusions regarding the choice and dose of drugs, time suitable for administration, or effect of analgesic infusions. In this regard, various studies have compared the intravenous infusions of lignocaine and dexmedetomidine for analgesia in gynecological laparoscopy, elective abdominal surgeries, and diagnostic laparoscopy. However, only intraoperative infusions of lignocaine and dexmedetomidine were used in these studies, and these were discontinued in the postoperative period. The potential analgesic effects of these drugs would be more, if the infusions were continued postoperatively as well.

In the present study, we designed a randomized clinical trial to evaluate the analgesic efficacy of intraoperative and postoperative infusions of intravenous lignocaine and intravenous dexmedetomidine for postoperative pain relief in total laparoscopic hysterectomy. The patients were also evaluated for any adverse effects associated with the infusion of these drugs.

AIMS AND OBJECTIVES

To compare the efficacy of intravenous infusion of lignocaine and dexmedetomidine in terms of:

1. Postoperative pain relief as assessed by visual analogue scale
2. Postoperative opioid consumption

REVIEW OF LITERATURE

Hysterectomies are the commonest gynecological surgeries performed globally.[20] In two-thirds of the cases, uterine fibroid is the main etiology.[21] In recent years, hysterectomies have advanced from open to laparoscopic approaches, due to various advantages - smaller incision, better visualization of pelvic anatomy and access to uterine vessels, reduced morbidity in terms of lesser blood loss, wound infections, postoperative pain, shorter hospital stay, and faster resumption of normal activities.[22]

However, laparoscopy has associated complications- pain, lower abdominal discomfort, shoulder pain, gastrointestinal tract disorders ranging from transient change in bowel function – constipation, decreased bowel frequency to de novo irritable bowel syndrome, lower limb venous thrombosis, and life-threatening pulmonary embolism.[22,23,24] Though laparoscopic surgeries result in less pain than open surgeries, many patients undergoing these procedures still experience high levels of perioperative pain along with many instances of referred pain.[25] Thus, pain control after total laparoscopic hysterectomy is often difficult, which leads to increased opioid use and delayed discharge from the hospital, despite being a minimally invasive technique.[26]

Choi et al conducted a study to comprehend the pain characteristics after total laparoscopic hysterectomy. They found that shoulder pain developed in 90% of patients, and peaked at postoperative 24 hours. Most patients reported only regarding abdominal pain, as they considered the shoulder pain unrelated to surgery. In the abdomen, two types of pain were experienced. Incisional pain was felt as a pricking sensation with relatively low intensity. Visceral pain was very intense and heavy/dull inner pain, and was associated with intestinal mobility and potentiated by the gaseous intestine. Incisional and visceral pains were intense 30 min after surgery, gradually decreasing thereafter. Visceral pain dominated over incisional pain constantly for postoperative 72 hr. 90% patients also experienced

perineal pain which was described as discomfort not pricking, however in 30% of patients, perineal pain was more unbearable as compared to abdominal pain.[7]

Abdominal pain in total laparoscopic hysterectomy occurs due to incision, stretching of the intra-abdominal cavity, tissue manipulation, blood left in the abdomen, and dissection of the pelvic region.[7] Shoulder pain in laparoscopic hysterectomy is a referred pain resulting from diaphragmatic irritation, mediated by the phrenic nerve (C3-5), which innervates the diaphragmatic pleural surface. Diaphragm irritation occurs due to H_2CO_3 conversion from CO_2, sub-diaphragmatic CO_2 entrapment, and retained fluid or blood. Moreover, shoulder pain after total laparoscopic hysterectomy may be intensified by intraoperative head down position and external compression.[8]

Analysis and measurement of pain is a difficult task since pain is a subjective sensation.[27] There is a disparity in the experience or feeling of pain among different individuals.[28] Various pain measurement tools have been formulated, depending upon the study design and the patient population. Single dimensional pain measurement tools are most frequently used. These include- visual analogue scales (VAS), categorical verbal rating scales (VRS), and categorical numerical rating scales (NRS). Multidimensional pain measurement tools are McGill Pain Questionnaire, and the Brief Pain Inventory.[29]

The visual analogue scale is a validated, subjective measure for acute and chronic pain. In this, scores are recorded by making a handwritten mark on a 10-cm line that represents a spectrum between “no pain” and “worst pain.” “ no pain” on the left end (0 cm) of the scale and the “worst pain” on the right end of the scale (10 cm). The patient rates the degree of pain. An essential prerequisite for accuracy of this scale is the visual and motor coordination of patient.[30]

Adequate management of postoperative pain is very important for the early discharge of patient and his resumption to normal activities.

Researchers have been investigating various agents and their combinations to improve postoperative pain control. Traditional therapies for postoperative analgesia have been opioids and NSAIDs.[31] However, opioids are not very effective in mitigating visceral/ dull pain. In addition to this, opioids result in psychological addiction and adverse effects, like nausea, vomiting, sedation, dizziness, constipation, and respiratory depression- all of which delay patient discharge. NSAIDs display analgesic, anti-inflammatory, and antipyretic properties. So they are widely used in postoperative analgesia.[31] However, they still cause gastrointestinal mucosal damage, platelet, and renal tubular dysfunction.[32]

Lirk et al conducted a systematic review of 56 randomized controlled trials to evaluate available literature on the management of pain after laparoscopic hysterectomy.[33] The researchers concluded from this study that NSAIDS reduced opioid consumption but their effects on mobilization and opioid-related side effects were unclear.[33] Dexamethasone reduced postoperative opioid consumption, nausea, and vomiting, but does not reduce pain scores.[33] Dexmedetomidine, an alpha-2-agonist, prolonged the time to rescue analgesia by, on average, 11 min as compared with placebo when given in a dose of 1 mcg/kg body weight.[34] It also decreased the number of patients requiring rescue analgesics in the PACU.[34] However limited studies were conducted on alpha-2 agonists so far. Gabapentinoids like pregabalin have opioid-sparing effects, but may cause dizziness, blurred vision, and headaches, especially at higher doses.[35] Inconsistent evidence was found in the studies investigating transversus abdominis plane block.[33] Limited evidence was found for intraperitoneal and port-site infiltration of local anesthetics in laparoscopic hysterectomy.[34] Measures to lower peritoneal insufflation pressure or humidify or heat insufflated gas seem to reduce the incidence of shoulder pain, but not abdominal pain.[34] Analgesic adjuncts like ketamine and intravenous lignocaine infusions have been suggested as potential

options.[36] However, the benefit of adding these drugs to the recommended pain management regimen in laparoscopic hysterectomy has been inadequately evaluated.[36]

Various studies regarding different non-opioid analgesic regimens were done by Blanton et al, Tulandi et al, Takmaz et al, and Hoskote but convincing conclusions have been difficult to draw regarding postoperative pain control in laparoscopic hysterectomy.[34-37]

Gibbison et al, Luo et al, Vadivelu et al, and Puntillo et al conducted an analysis of routes of administration of analgesics in the immediate postoperative period. [38-41] These studies concluded that intravenous formulations of drugs had faster onset time, higher plasma levels, thus more efficiency than the oral forms. Despite higher costs, they were more useful in the immediate postoperative period especially in case of postoperative nausea and vomiting. The intramuscular route was strongly discouraged. The rectal route must be preferred only in the absence of other routes. The epidural route had been effectively used but was associated with more incidence of pruritis, urinary retention, and hypotension compared to systemic analgesics. Peripheral nerve blocks had been increasingly used, but potential risks like nerve injury, bleeding, and infection may limit their use.[38-41]

Some authors have studied and advocated the use of alpha-2 agonists as adjuvants for postoperative pain management. Dexmedetomidine is highly selective and specific for alpha 2-receptors with an α_2: α_1 ratio of 1620:1(about 8 times more than clonidine). [42] Analgesic effects of dexmedetomidine are mediated by spinal and supraspinal sites. At these sites, dexmedetomidine causes hyperpolarization of interneurons and suppresses pain transmission by inhibiting the release of neurotransmitters such as glutamate and substance P, which alter the perception of pain. Sedative and hypnotic effects of dexmedetomidine are mediated through activation of central pre-and postsynaptic α_2-receptors in the locus coeruleus, where it increases the activity of inhibitory gamma-

aminobutyric acid neurons in the ventral preoptic nucleus.[42-46] The sedative effect is concentration-dependent, with plasma concentrations between 0.2 and 0.3 ng/mL resulting in significant and rousable sedation. Peripheral actions of the drug are manifested when postsynaptic alpha-2 adrenoceptors are activated. There occurs sympathetic inhibition of the medullary vasomotor center upon activation of alpha 2 receptors. This brings about a dose-dependent reduction in the levels of plasma catecholamines (maximum 89%), bradycardia, and hypotension. Alpha 2 adrenoceptors do not have a dynamic role in the respiratory center, consequently, dexmedetomidine throughout a broad range of plasma concentrations (up to 8 ng/ml), has negligible effects on the respiratory system. When dexmedetomidine is injected rapidly, in a bolus dose or a fairly large dose (>1000 mcg/kg), blood pressure shows a biphasic variation. An initial short hypertensive phase is observed that is mediated by alpha-2 beta-adrenergic receptors on the peripheral vascular smooth muscle. This effect usually lasts for about 5 to 10 min. It is followed by a hypotensive phase mediated by alpha 2A adrenergic receptors inhibiting the sympathetic release of catecholamines and the increased vagal activity. The initial hypertensive phase can be attenuated to some extent by using a slow infusion for over 10 or more minutes. The recommended dose range of intravenous dexmedetomidine is 0.2 to 0.7 mcg/kg/hr for no more than 24 hours. Side effects include hypotension, bradycardia, arrhythmias and heart blocks.[42- 46]

Various studies have been conducted to evaluate the effect of intraoperative dexmedetomidine infusion for postoperative pain relief. A study was done by Ge et al where they studied the efficacy of dexmedetomidine in 64 patients undergoing abdominal hysterectomy.[47] Patients were divided into two groups. One group received saline and the other group received an equivalent amount of dexmedetomidine, intraoperatively, as adjuvants to general anesthesia. During surgery, patients in the dexmedetomidine group had a lower bispectral index (BIS)

value, which indicated a deeper anesthetic state and a higher sedation score immediately after extubation than patients in the saline group. During the first 24 hours post-surgery, the dexmedetomidine group consumed less morphine and had lower scores on a visual analog scale than the controls from the saline group. The conclusion was that intraoperative dexmedetomidine decreased anesthetic and analgesic requirements and improved patient recovery following hysterectomy.[47]

Aho et al studied the analgesic efficacy of intravenous dexmedetomidine in laparoscopic tubal ligation.[48] Ninety-six women undergoing laparoscopic tubal ligation were randomized into 4 groups to receive intravenously either 0.2 or 0.4 mcg/kg of dexmedetomidine, 60 mcg/kg of oxycodone, or 250 mcg/kg of diclofenac for postoperative pain in the recovery room. They concluded that dexmedetomidine relieves pain and reduces opioid drug requirements but is associated with sedation and a high incidence of bradycardia.[48]

A study was conducted by Naik et al regarding effects of dexmedetomidine on postoperative opioid consumption and pain after major spine surgery.[49] They compared the efficacy of dexmedetomidine (1mcg/kg loading dose followed by a continuous infusion of 0.5 mcg/kg/h) and saline. There was no difference in pain score or opioid consumption in the first 24 hours. There was increase in incidence of bradycardia and use of phenyephrine among the dexmedetomidine group. The data suggested that the administration of dexmedetomidine is not effective in reducing opioid consumption or improving postoperative pain scores in spine surgery.[49]

The use of intravenous dexmedetomidine and paracetamol was studied by Sarkar et al in patients undergoing laparoscopic surgeries.[50] Group D received intravenous dexmedetomidine 1mcg/kg over 10 min followed by 0.2-0.7 mcg /kg/hr and Group P received intravenous paracetamol 15 mg/kg prior to extubation. More patients in group D required rescue analgesia than patients in P group. VAS scores were similar in both

groups. Median time at which the first dose of rescue analgesia was administered in group P was longer. Bradycardia and hypotension was higher in group D. They noted that paracetamol was superior to dexmedetomidine for analgesia in short surgical procedures.[50]

Efficacy of postoperative intravenous infusions of dexmedetomidine have also been studied. Abd El Megid et al conducted a study to evaluate the analgesic and sedative properties of dexmedetomidine infusion after uvulopalatopharyngoplasty. Group D received a loading dose of intravenous dexmedetomidine 1mcg/kg 30 min before the anticipated end of surgery, followed by a continuous infusion at a rate of 0.6 mcg/kg/hr for 24hr. Group P received same amount of saline. Pain scores were significantly greater in group P during the first 2 hr. Time to first analgesic request was significantly longer and postoperative morphine consumption was lesser in group D. Sedation scores were similar between the 2 groups at all observation times. Fewer patients in group D experienced nausea and vomiting and there was no bradycardia, hypotension, or respiratory depression. Thus, continuous infusion of dexmedetomidine reduced postoperative morphine consumption without affecting hemodynamics or ventilatory parameters.[51]

Priye et al did a study on 64 patients using dexmedetomidine infusion for postoperative pain relief after cardiac surgery. Group A received a 12 hr infusion of normal saline and group B received a 12 hr infusion of dexmedetomidine 0.4 mcg/kg/hr. Pain scores, fentanyl consumption, and delirium were lesser in Group D. Statistically significant but clinically unimportant sedation was noted at 6 and 12 hr in group D, with stable hemodynamics. Conclusion was made that dexmedetomidine decreases pain, opioid consumption without undesirable hemodynamic effects.[52]

Dhawan et al compared two different doses of dexmedetomidine for analgesia in abdominal hysterectomy. In group 1, 0.6 mcg/kg loading dose of dexmedetomidine intravenously followed by 0.3 mcg/kg/hr maintenance dose was given while in group 2, 0.4mcg/kg loading followed by

0.3mcg/kg/hr maintenance dose was given. Postoperative pain relief, along with sedation and hypotension was more in group 1.[53]

Ye et al conducted a study on 120 patients dividing them into 4 groups for investigating the optimal dose of dexmedetomidine to maintain hemodynamic stability, prevent cough and minimize postoperative pain in laparoscopic cholecystectomy. D_1, D_2, D_3, and NS groups were administered dexmedetomidine 0.4, 0.6, 0.8μg/kg and normal saline respectively in the intraoperative period. The authors observed that D2 and D3 groups had smaller fluctuations in hemodynamic parameters, lower incidence of cough, better pain scores, and lower tramadol requirements than the D1 and NS groups. Extubation time was more in D3 than D1 and D2. They concluded that 0.6 mcg/kg dose of dexmedetomidine can offer hemodynamic stability, decrease cough during emergence and relieve postoperative pain of patients.[54]

Rabie et al compared three intraoperative doses of dexmedetomidine 0.2 mcg/kg/hr, 0.4 mcg/kg/hr and 0.6 mcg/kg/hr in patients undergoing laparoscopic cholecystectomy and concluded that postoperative analgesic requirements were lesser in 0.6 mcg/kg/hr group.[55] Dailey et al used a dexmedetomidine infusion of 0.7 mcg/kg/hr for > 24 hours for treatment of alcohol withdrawal.[56] They concluded that dexmedetomidine reduced need for benzodiazipines but also resulted in hypotension in half of the patients.

Castillo et al administered dexmedetomidine infusion 0.2-1.5 mcg/kg/hr with a maximum average dose of 1mcg/kg/hr in critically ill patients and found that this dose caused significant adverse effects like bradycardia and hypotension in 50% of the patients.[57] Ebert et al observed that progressively increasing concentrations of dexmedetomidine resulted in a decrease in HR, and a biphasic (low, then high) dose-response relationship for BP and a progressive increase in sedation and analgesia, with minimal respiratory changes.[58]

Lignocaine is a local anesthetic that displays rapid onset of action, moderate potency, and duration. Lignocaine is classified as a Class 1-B antiarrhythmic. It acts directly, occludes the sodium channels in the cardiac muscle, inhibits action potential, and reduces the duration of the effective refractory period in purkinje fibers and ventricular muscles (except atrial fibers). This stabilizes the cardiac cell membrane, curbs the automaticity of firing at the atrioventricular node (except SA node), and abolishes the ectopic foci from damaged and excitable cells by antagonizing phase IV depolarization. During laryngoscopy, the sympathetic activation results in elevated cerebral blood flow and raised intracranial pressure. Lignocaine dulls this sympathetic response. Lignocaine relaxes bronchial smooth muscles, so reflex bronchoconstriction that may occur after airway manipulation is prevented.[59-63] Based on evidence from various studies, Epie et al, concluded that the most widely reported and clinically effective dose range of intravenous lignocaine appears to be from 1 to 2 mg/kg/hr.[64] Side effects include nausea, lightheadedness, tinnitus, circumoral, and tongue numbness. visual disturbances, convulsions.[59-63] Szmuck et al, in their study on effect of lignocaine on pain perception, observed that high dose lignocaine infusion (5mg/kg/hr) resulted in deep sedation in all patients.[65] The analgesic action of intravenous lignocaine has been evaluated by various studies. Murthy et al studied the effect of intravenous lignocaine on hemodynamic response and postoperative analgesia in laparoscopic cholecystectomy.[66] In group A, 0.9% normal saline was used as a placebo. In group B, 1.5 mg/kg 2% lignocaine bolus, and infusion of 1.5 mg/kg/hr till 1 hr postoperatively was given. Hemodynamic response to intubation and extubation was measured by heart rate and mean blood pressure. Postoperative pain was measured by VAS. They concluded that perioperative intravenous infusion of lignocaine attenuates hemodynamic response during the intubation and extubation of the trachea, and also increases the mean pain-free period postoperatively.[66]

Dewinter et al observed the effect of lignocaine infusion in posterior spinal arthrodesis. 70 patients were randomized into two equal groups. Group received lignocaine- bolus 1.5 mg/kg and maintenance infusion 1.5 mg/kg/hr continued until six-hour postoperatively. Group II received saline. Lignocaine did not decrease postoperative pain scores, morphine requirements, nausea and vomiting, perioperative inflammation, time to recovery of intestinal function, and hospital length of stay. Thus it was noted that intravenous lignocaine has no analgesic benefits in spinal arthrodesis patients.[67]

Continuous postoperative infusions of intravenous lignocaine have also been studied. Ho et al studied the effect of lignocaine infusion for pain relief in open colorectal surgery. 58 patients were randomized into two groups. The lignocaine group received 1.5 mg/kg bolus followed by 1 mg/kg/hr infusion for 48 hours and control group received saline. After surgery, time to first bowel movement and flatus, postoperative pain scores and fentanyl consumption were assessed for 72 hours. They noted that a 48 hr low dose intravenous lignocaine infusion did not significantly decrease postoperative pain scores, speed the return of bowel movement and length of hospital stay. However, fentanyl consumption was significantly lower in the lignocaine group from 24 hrs onwards, and was 40% lower than placebo group at 72 hours.[68]

Chamaidi et al conducted a systematic review to evaluate efficacy of intravenous lignocaine in laparoscopic colectomies. 8 studies and 407 patients were included in this meta-analysis. They interpreted that intravenous lidocaine did not improve hospitalization duration, morphine consumption, perioperative bowel function, or the overall complication rates. However, high heterogeneity levels were identified. They concluded that lignocaine did not improve rehabilitation after laparoscopic colectomies.[69]

Tauzin et al evaluated the effects of intravenous lidocaine after laparoscopic nephrectomy. Group L (n=22) were given intravenous

lignocaine 1.5 mg/kg/hr intraoperatively and 24 hours postoperatively. Group P received saline. Post-operative pain scores, opioid consumption and extent of hyperalgesia were measured. Lidocaine significantly reduced morphine consumption, post-operative pain scores and hyperalgesia extent on post-operative day 1, day 2, and day 4. They inferred that intravenous lignocaine could reduce post-operative morphine consumption and improve post-operative pain management and post-operative recovery after laparoscopic nephrectomy.[70]

Efficacy of lignocaine on pain relief in laparoscopic cholecystectomy was studied by Lahiri et al. 120 patients were randomized into 2 groups to receive intraoperative intravenous lignocaine 1.5 mg/kg bolus then 3 mg/kg/hr till extubation; or equal amount of saline. Postoperative requirement of fentanyl was significantly lower in lignocaine group compared to saline group. They concluded that intravenous lignocaine effectively improves recovery and reduces postoperative fentanyl requirement, thereby is an inexpensive and safe method of postoperative analgesia.[71]

Intravenous lignocaine for pain relief and incidence of side effects was studied by Augustine et al in laparoscopic cholecystectomy. [72] 40 patients were randomized into two groups A and B. Group A received saline and group B received 2mg/kg/hr lignocaine infusion intravenously till the end of the surgery. Postoperative pain was assessed by NRS score at immediate postoperative period, 2nd, 4th, 6th, 8th, 10th, 12th and 24th hours. Time at which first rescue analgesia was requested, total analgesic requirements, mean NRS score and side effects were noted. The researchers observed that at every time interval, patients in lignocaine group had delayed time to request for rescue analgesia, less analgesic requirements, mean NRS and no side effects or signs of toxicity. They concluded that lignocaine infusion is an efficient, safe and cost-effective armamentarium in postoperative analgesia.[72]

Ibrahim et al studied the effect of intravenous lignocaine infusion on long term postoperative pain intensity for 3 months in spinal fusion surgery. 40 patients were randomized into 2 equal groups.[73] Patients in the lignocaine group received IV lidocaine 2.0 mg/kg bolus and infusion 3.0 mg/kg/hr until the end of surgery. Patients in the control group received an equal volume of normal saline. Lignocaine significantly reduced the postoperative pain score (VAS) for up to 3 months and morphine consumption in 1st 24 hours postoperative period. It also significantly prolonged the time to first request for additional analgesia. Thus, intra-operative lidocaine, given intravenously as a bolus followed by an infusion, significantly decreased long term postoperative pain intensity.[73]

Patients undergoing bimaxillary surgery experienced lesser postoperative pain, analgesic consumption and facial swelling, when administered an intravenous lignocaine infusion, as studied by Lee et al.[74] Kim et al evaluated intravenous lignocaine infusion in patients undergoing lumbar surgery and concluded that VAS scores and fentanyl consumption was significantly lower in lignocaine group upto postoperative 48 hrs along with a lower incidence of postoperative nausea and vomiting and decreased length of hospital stay in this group.[75] Page et al in their study concluded that IV lignocaine infusion was effective for intractable pain in Ewing's sarcoma, where the pain score by numerical rating scale(NRS) came down from 8/10 to 4/10 after first infusion.[76]

Various studies have compared the efficacy of dexmedetomidine versus lignocaine for postoperative pain relief. The efficacy of IV dexmedetomidine versus lignocaine for abdominal gynaecological surgery was studied by Rekatsina et al, where they divided 91 patients into 3 groups.[77] Dexmedetomidine (bolus: 0.6 mcg/kg, infusion: 0.6 mcg/kg/hr), or lignocaine (bolus: 1.5 mg/kg, infusion: 1.5 mg/kg/ hr), or NaCl 0.9% were used in Group I, II, III respectively, intraoperatively. Pain scores were comparable in all 3 groups. Group II had maximum morphine sparing effect amongst 3 groups, Group I had least incidence of postoperative

nausea and maximum hypotension. It was concluded that both dexmedetomidine and lidocaine could be useful adjuvants for analgesia after abdominal surgery. Lignocaine reduced postoperative opioid consumption, while dexmedetomidine prevented early postoperative nausea. However, hypotension and the need for vasopressors was common with both agents, especially with dexmedetomidine.[77]

Menshawi et al studied efficacy of dexmedetomidine versus lignocaine in abdominal gynecological surgeries under general anesthesia.[78] They divided 90 patients into three equal (n=30) groups. Group L received lignocaine (1.5 mg/kg loading, 2 mg/kg/hr infusion), group D received dexmedetomidine (1 mcg/kg loading, 0.5 mcg/kg/hr infusion), and group C received isotonic saline 0.9%. Postoperative blood pressure and heart rate was lower in group L and D than group C with no difference amongst the two groups. Time to 1st postoperative analgesic was maximum in Group D. The inference was that both dexmedetomidine and lignocaine could be a useful adjuvant to general anaesthesia in patients undergoing abdominal gynecological surgeries. However, dexmedetomidine had longer time to the first postoperative analgesic demand than that of lignocaine with no significant difference between both agents on intraoperative analgesic demand.[78]

Cho et al studied lignocaine vs. dexmedetomidine on reduced consumption of postoperative analgesics after laparoscopic cholecystectomy.[79] 84 patients were randomized to receive IV lignocaine 1.5 mg/kg bolus then 2 mg/kg/hr infusion (group L) or 1 mcg/kg bolus, then 0.4 mcg/kg/hr dexmedetomidine(group D) till end of surgery. Placebo group received saline. No significant difference was observed in VAS score among the groups during the first 24 hr. Fentanyl consumption was less in groups L and D compared to group N. The inference was both drugs reduced postoperative fentanyl consumption with no difference in analgesic sparing effect.[79]

Xu et al studied the role of intraoperative lignocaine and dexmedetomidine and their combination on IL-1, IL-6, TNF-α, hemodynamics and VAS in patients undergoing laparoscopic hysterectomy and the study resulted that the combination of lidocaine and dexmedetomidine alleviated the inflammatory responses, decreased postoperative pain, and led to fewer PONV after laparoscopic hysterectomy. There was no difference in VAS, fall in blood pressure between lignocaine and dexmedetomidine group, while fall in heart rate was more in dexmedetomidine group than lignocaine group.[80]

Anis et al did a study using intraoperative lignocaine and dexmedetomidine infusion for hemodynamic stability and recovery profile after diagnostic laparoscopic gynecologic surgeries. Group L received lignocaine 1.5 mg/kg bolus and 2 mg/kg/hr infusion. Group D received dexmedetomidine 0.5 mcg/kg bolus and 0.4 mcg/kg/hr infusion. Group D showed more fall in mean heart rate but similar changes in blood pressure and more sedation. Group L showed better postoperative pain scores but similar pethidine consumption. They noted that lignocaine is an effective modality similar to dexmedetomidine, to control the hemodynamic response during surgery. It reduces the postoperative analgesic requirements without significant respiratory impairment.[81]

Kumari et al evaluated intraoperative lignocaine (1.5 mg/kg bolus over 10 minutes followed by 2 mg/kg/hr) versus dexmedetomidine (1 mcg/kg bolus followed by 0.4 mcg/kg/hr) in laparoscopic cholecystectomy. Postoperative sedation score, analgesic sparing, nausea, vomiting, VAS score over 24 hours were comparable in both the groups. They interpreted that both drugs were effective and safe adjuvants but the postoperative recovery profile was better with dexmedetomidine infusion and it maybe considered a superior adjuvant over lignocaine in outpatient laparoscopic surgery.[82]

Mohammed et al compared intraoperative 0.3-0.5 mg/kg/hr lignocaine and 0.3-0.5 mcg/kg/hr dexmedetomidine infusions for pain relief in lumbar

fixation surgery and concluded that dexmedetomidine showed better pain scores and more analgesic sparing effect than lignocaine.[83]

Andjelkovic et al compared effect of intraoperative infusions of lignocaine (1.5 mg/kg/hr) and dexmedetomidine (0.5 mcg/kg/hr) on pain relief after laparoscopic intestinal resection. They observed that VAS score was lower in lignocaine group than dexmedetomidine group on the day of surgery, with no difference in fentanyl consumption in postoperative period.[84]

Shivaji et al randomized 96 patients undergoing robotic abdominal hysterectomy into 4 groups. Groups received lignocaine infusion (1.5 mg/kg loading, 2 mg/kg/hr infusion) (Group I), dexmedetomidine infusion (1 mcg/kg loading, 0.6 mcg/kg/hr infusion) (Group 2), lidocaine (1.5 mg/kg loading, 2 mg/kg/hr infusion), and dexmedetomidine infusions (1 mcg/kg loading, 0.5 mcg/kg/hr infusion) (Group 3), and normal saline 10 mL loading, 1 mL/kg/hr infusion) (Group 4). The VAS score, fentanyl consumption, time to return of bowel sounds and passage of flatus was lower in Groups 2 and 3 compared to Groups 1 and 4, and lesser in group 1 than 4. They concluded that combined infusion of lignocaine and dexmedetomidine decreased postoperative pain, fentanyl consumption, and improved quality of recovery score after surgery.[85]

Thus, a thorough review of literature reveals that there still is no consensus on the role of dexmedetomidine and lignocaine infusion in postoperative pain management. Most of the studies have compared intraoperative infusion of dexmedetomidine and lignocaine and reported variable results. It is plausible that continuing the infusions in postoperative period can result in better pain management and reduced opioid requirements. Thus, the present study aims to compare the perioperative efficacy of IV lignocaine versus IV dexmedetomidine for postoperative pain relief in elective total laparoscopic hysterectomy cases.

MATERIALS AND METHODS

SOURCE OF DATA

The planned study was conducted in the department of Anaesthesiology at Dayanand Medical College and Hospital, Ludhiana as a randomised double blinded study on a total of 60 patients scheduled for total laparoscopic hysterectomy under general anaesthesia after getting approval by the Ethics Committee of the Hospital.

METHOD OF COLLECTION OF DATA

PREANAESTHETIC CHECKUP

A thorough pre anaesthetic checkup including a detailed complete history, general physical and systemic examination was performed a day prior to surgery. Baseline investigations like complete hemogram, serum electrolytes, coagulogram, random blood sugar, ECG, chest X-ray and other indicated investigations were done prior to surgery. Patients were educated about the application of visual analogue scale and that they could request for additional analgesic whenever they complained of pain and written informed consent was taken.

Inclusion criteria -

Patients of age between 35-60 years belonging to ASA physical status I and II scheduled for elective total laparoscopic hysterectomy under general anaesthesia.

Exclusion criteria- Following patients were not included in the study:

- Consent refusal.
- Patients on anti-arrythmic drugs.
- Patients with known history of coronary artery disease, liver disease.
- Allergic to a local anesthetic.
- Psychiatric patients.
- Inability to comprehend VAS.

Group allocations: Sixty patients were randomly allocated into two groups- A and B of 30 patients each, according to computer generated random numbers maintained in sequentially numbered, opaque envelopes. The patients were started on intraoperative infusions of the study drug which were continued in the postoperative period for upto 24 hours.

Group A patients received IV bolus of lignocaine of 1.5 mg/kg over 10 min followed by 1 mg/kg/hr infusion for 24 hours.

Group B patients received IV bolus of dexmedetomidine of 1 mcg/kg over 10 min followed by 0.6 mcg/kg/hr infusion for 24 hours.

A person not involved in the postoperative management of the patient prepared the study drugs in a sterile syringe and administered the drugs to the patient. The candidate, blinded to the infusion of study drug, recorded the postoperative vitals, VAS scores and pain relief data up to 24 hours following the surgical procedure.

PREMEDICATION

Prior to the surgery, patient was kept fasting for a period of 8 hours. She was given tablet Pantoprazole 40 mg and tablet Alprazolam 0.5mg on night before surgery with small sip of water.

ANAESTHESIA TECHNIQUE:

The study was conducted on American Society of Anesthesiologists (ASA) I, II patients posted for total laparoscopic hysterectomy. After arrival of patient to the operating room, she was positioned on the operating table in supine position and an IV line was secured and IV fluids were started. Routine monitoring including pulse oximetry, electrocardiography (ECG), non invasive blood pressure (NIBP), end tidal carbon dioxide ($EtCO_2$) was done and baseline parameters were noted.

Ten minutes before induction of anaesthesia, in group A patients, IV bolus of lignocaine 1.5mg/kg diluted to total volume of 20 ml with normal saline in a 50ml syringe was administered over a period of 10 minutes. Then, an IV infusion of lignocaine 1mg/kg/hr diluted in normal saline, in a 50 ml

syringe was prepared. It was administered through an infusion pump, during entire surgical procedure and for first 24 hours after surgery. Group B patients received IV bolus of 1 mcg/kg of dexmedetomidine diluted to a total volume of 20 ml with normal saline, in a 50 ml syringe, 10 minutes before the induction of anaesthesia, over a period of 10 minutes. Thereafter an IV dexmedetomidine infusion of 0.6 mcg/kg/hr diluted in normal saline, in a 50 ml syringe, throughout surgery and for first 24 hours after surgery was administered.

Patients were administered intravenously injection(inj.) metoclopramide 10mg, inj. fentanyl 2 mcg/kg, and inj. glycopyrrolate 0.2mg. All patients were pre oxygenated with 100% oxygen for 3 minutes. For anaesthesia induction, inj. propofol 1.5-2 mg/kg IV was injected slowly till there was loss of verbal response. Loading dose of atracurium 0.5mg/kg IV was given. Direct laryngoscopy was performed three minutes later and trachea was intubated with an appropriate sized cuffed endotracheal tube. Cuff was inflated and placement of tube in trachea was confirmed by bilateral equal air entry on chest auscultation and end tidal CO_2. The patients were mechanically ventilated with ventilator using volume controlled mode of ventilation. Desflurane was used to maintain anaesthesia titrated according to the hemodynamic parameters of the patient.

The entire surgical procedure done in the study was performed by a single surgeon thus limiting surgical variation.

During surgery, boluses of inj. atracurium 0.1 mg/kg were given for the maintenance of relaxation, while monitoring the heart rate, blood pressure, respiratory rate, SpO_2. Inj. fentanyl 0.5 mcg/kg was given after every 1 hour.

Inj. diclofenac sodium 75 mg intravenous first dose, in 100 ml normal saline, was given 30 minutes before expected extubation and then every 8 hourly as a part of the multimodal analgesia regimen. At the end of surgery, inj. ondansetron 0.1mg/kg intravenous was given. After closure of the skin all anaesthetic agents were stopped.

Trachea was extubated after administering inj. neostigmine 0.05mg/kg IV and inj. glycopyrrolate 0.01 mg/kg IV, at the discretion of the attending anaesthesiologist and when respiratory efforts of patient became regular and patient became responsive.

Patients were transferred to post anaesthesia care unit (PACU) and this time was labelled as zero hour i.e. immediate postoperative period. In PACU, the infusion of the study drug was continued for 24 hours postoperatively. Patients also received inj. diclofenac sodium 75 mg IV 8 hourly in postoperative period.

During the first 24 hours in PACU, postoperative pain was assessed using Visual Analogue Scale (0-10). [Fig-A]

Visual analogue scale having 0 to 10 equidistant markings was shown and explained to patient at the time of pre- anaesthetic evaluation. Pain scoring was done by asking the patient to choose along the scale with 0 corresponding to 'no pain' and 10 corresponding to ' worst imaginable pain'. The intensity of pain felt by patient was scored at fixed intervals after surgery.

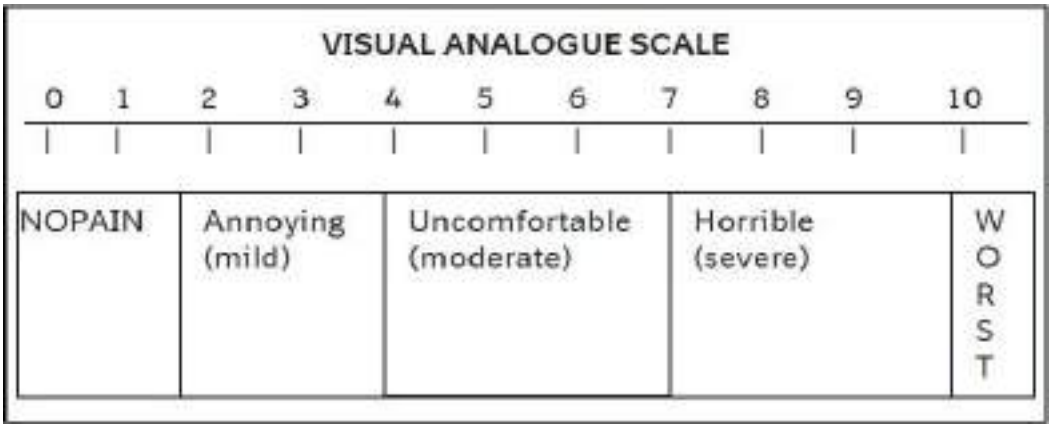

Fig-A: Visual analogue scale [30]

Whenever the patient complained of pain post operatively, a rescue analgesic - tramadol 50mg IV in 100 ml normal saline was administered, to maintain a VAS of ≤ 3 at rest. Dose and time of first rescue analgesic was noted. If patient still complained of pain even after 15 minutes of receiving tramadol, same doses were repeated up to a maximum of 100

mg in contiguous 4 hours or 400 mg in 24 hours. If patient still complained of pain, then fentanyl 1mcg/kg bolus dose was given as second rescue analgesic.

Bradycardia defined as heart rate less than 60 beats/min, was treated with intravenous atropine sulphate 0.01mg/kg.[86] Hypotension was defined as decrease of systolic blood pressure to < 80% of the baseline value or combination of two criteria i.e. systolic blood pressure < 100mmHg or a decrease to <80 % of the baseline.[87] It was treated by IV boluses of 100 ml of crystalloid fluids and ephedrine 6mg IV as required.

Sedation was assessed using Ramsay Sedation Score. [88]

1= patient is anxious and agitated or restless, or both

2= patient is cooperative, oriented and tranquil

3= patient responds to commands only

4= patient exhibits brisk response to light glabellar tap or loud auditory stimulus

5= patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus

6= patient exhibits no response

Number of times and total number of doses of first and subsequent rescue analgesic needed was also recorded. Any patient sleeping comfortably in bed at any time of observations was not disturbed and was considered pain free having VAS score of less than 4 at that time of observation.

Total amount of Postoperative analgesic consumption in 24 hours was calculated.

OUTCOME: The outcome of the study was evaluated in terms of

PRIMARY OUTCOME measures:

1. Post-operative VAS score
2. Total opioid consumption in 24 hours

SECONDARY OUTCOME measures:

1. Time of administration of first and subsequent rescue analgesic and number of times rescue analgesic needed to be given.

2. The adverse effects of the drugs such as nausea, vomiting, hypotension, sedation, bradycardia.

Sample size calculation: A post hoc power analysis was conducted using the software package, G* Power version 3.1.9.2 (Frank Faul, university kiel, Germany). The alpha level used for this analysis was $p < 0.05$ and beta was 0.20. Based on a previous report by Anis G et al [81] using VAS as the parameter, which is the primary outcome of our study. With an effect size of 1.01 and under the assumption of a two- sided alpha error of 0.05 and a power of 80%, the required number of patients for each group was calculated to be 60 patients.

Statistical analysis: Data was described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups was done using Student t-test and Mann Whitney U test for independent samples for parametric and non-parametric data respectively. For comparing categorical data, Chi square ($\chi 2$) test was performed and exact test was used when the expected frequency was less than 5. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations was done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

OBSERVATIONS AND RESULTS

The present study was conducted in a randomized, double-blinded manner in the department of anesthesiology, DMCH Ludhiana on a total of 60 adult female patients, between age group 35-60 years belonging to ASA grades I and II scheduled to undergo total laparoscopic hysterectomy under general anesthesia.

The study aimed to evaluate the comparative efficacy of intravenous infusion of lignocaine versus dexmedetomidine for postoperative pain relief in patients undergoing total laparoscopic hysterectomy. Patients were divided into two groups of 30 patients each, who were administered the study drugs intravenously, each diluted to make a volume of 20 ml, given over 10 min as a loading dose, and then diluted to make a volume of 50 ml, given as maintenance dose during the entire surgical procedure and the first 24 hours after surgery.

Group A- patients were treated with lignocaine 1.5 mg/kg loading dose followed by 1mg/kg/hr maintenance dose.

Group B- Patients were treated with dexmedetomidine 1 mcg/kg loading dose followed by 0.6 mcg/kg/hr maintenance dose.

Hemodynamic parameters, visual analog scores, total opioid consumption in 24 hours, time of administration of first and subsequent rescue analgesia and the number of times rescue analgesic needed, adverse effects of the drugs such as nausea, vomiting, bradycardia, and hypotension were noted at fixed intervals, in the immediate postoperative period, 1, 2, 3, 4, 5, 6, 8, 10, 12, 16, 20 and 24 hours after surgery. The observations of our comparative study are as follows:

DEMOGRAPHIC PROFILE

Table 1: Mean age distribution (years)

	Group A		Group B		t	p-value
	Mean	SD	Mean	SD		
Age(years)	45.37	5.56	44.93	5.85	0.294	0.770

The mean age of patients in group A was 45.37 ± 5.56 years and in group B was 44.93 ± 5.85 years. There was no statistically significant difference between the two groups with respect to age, the p value being 0.770.

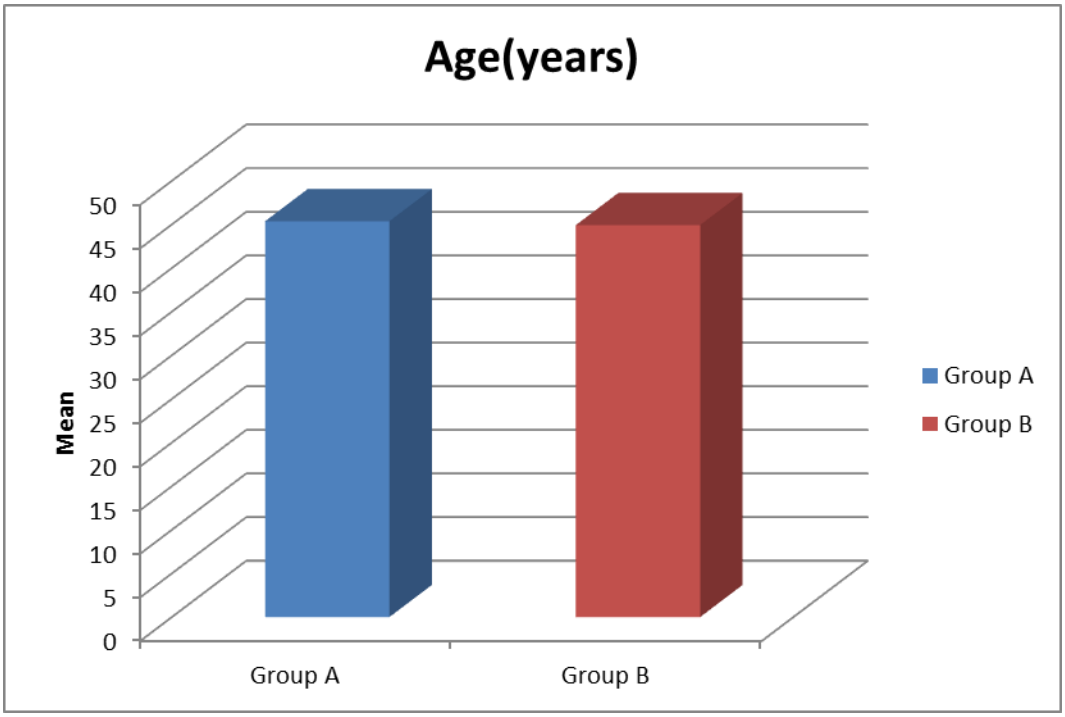

Figure 1: Mean age distribution (years)

Table 2. Mean height (cm)

	Group A		Group B		t	p-value
	Mean	SD	Mean	SD		
Height(cm)	160.01	3.18	160.43	2.74	-0.552	0.583

The mean height of patients in group A was 160.01 ± 3.18 cm and in group B, it was 160.43 ± 2.74 cm. Both the groups were statistically comparable with respect to height, p-value being 0.583.

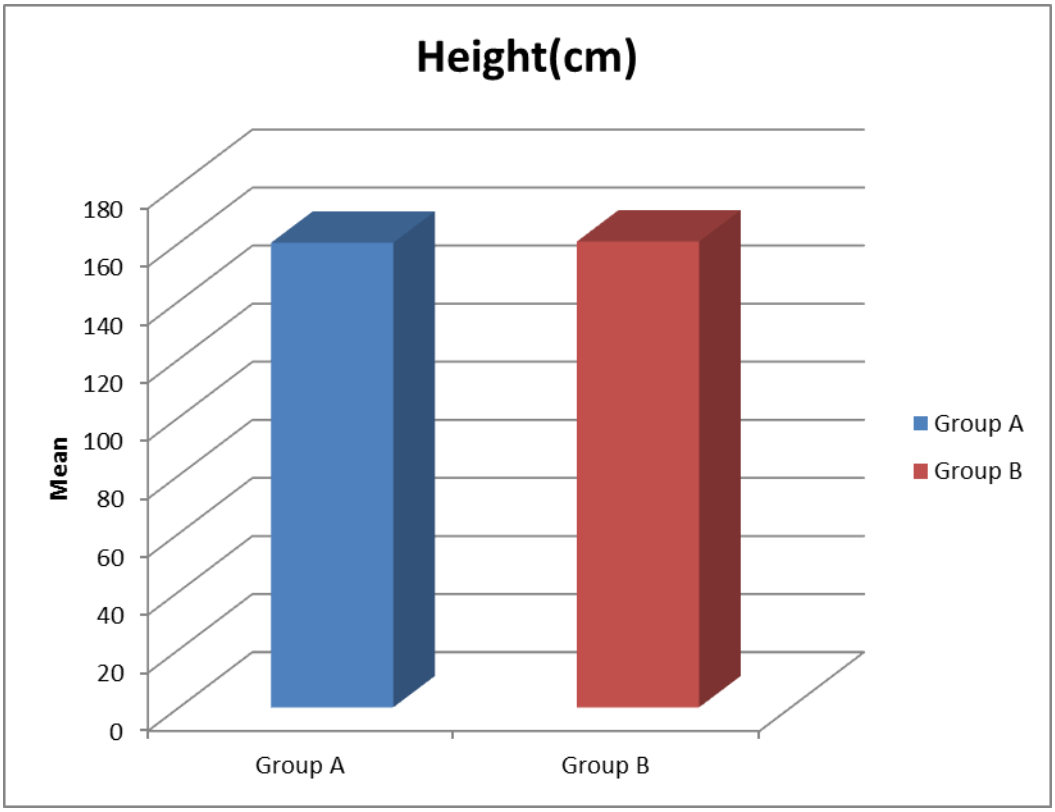

Figure 2. Mean height (cm)

Table 3. Mean weight (kg)

	Group A		Group B		t	p-value
	Mean	SD	Mean	SD		
Weight (kg)	64.70	4.71	67.33	6.61	-1.778	0.081

The mean weight of patients in group A was 64.70 ± 4.71 kg and in group B mean weight was 67.33 ± 6.61 kg. Therefore, the mean weight in both the groups was statistically similar, p-value being 0.081.

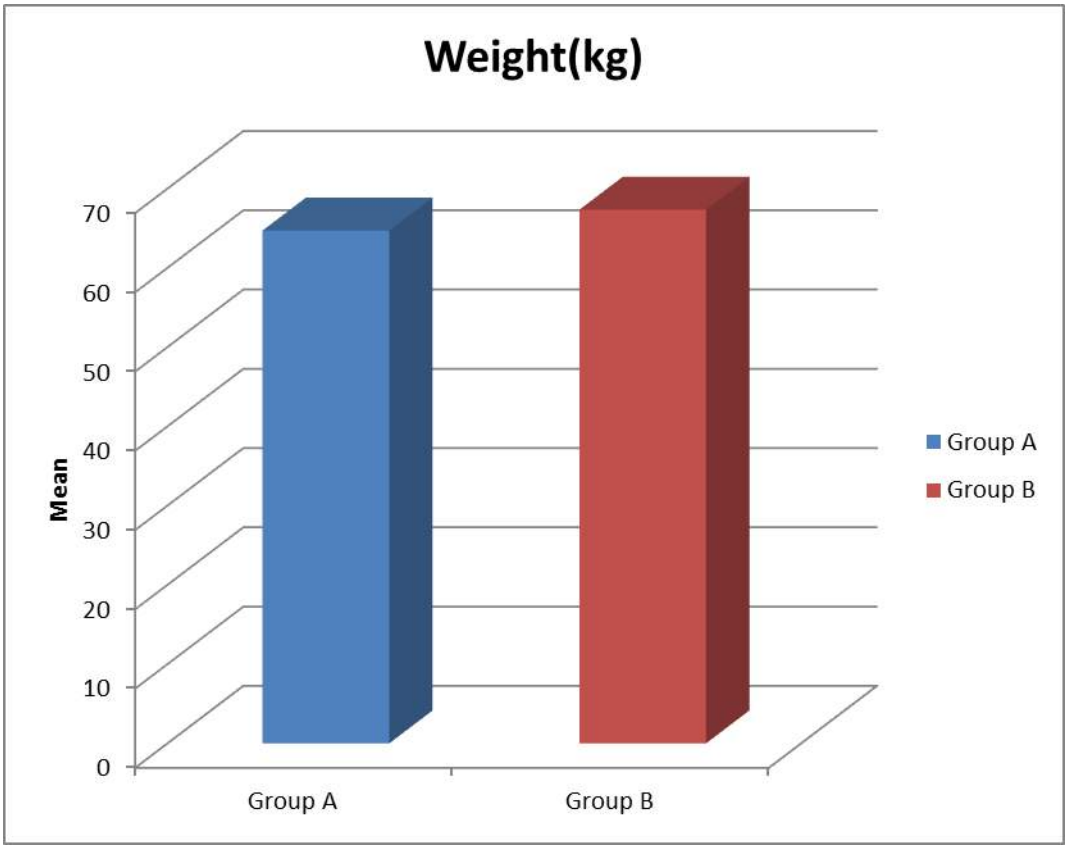

Figure 3. Mean weight(kg)

4. Mean BMI (kg/m^2)

	Group A		Group B		t	p-value
	Mean	SD	Mean	SD		
BMI (kg/m^2)	25.33	1.48	26.18	2.29	-1.699	0.095

The mean BMI of patients in group A was 25.33 ± 1.48 kg/m^2 and in group B it was 26.18 ± 2.29 kg/m^2. There was no statistically significant difference between the two groups with respect to BMI, p-value being 0.095.

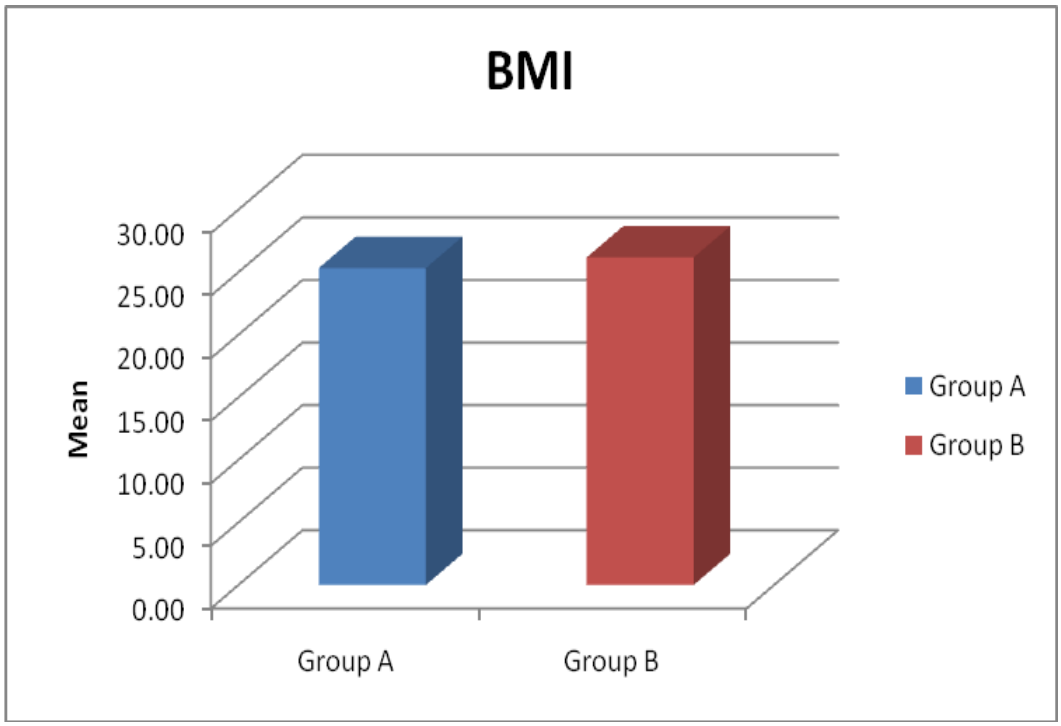

Figure 4. Mean BMI (kg/m^2)

5. ASA physical status

		Group		Total	p-value
		Group A	Group B		
ASA physical status	I	19	14	33	0.194
	II	11	16	27	
Total		30	30	60	

Both the groups were comparable with respect to ASA physical status (p value being 0.194)

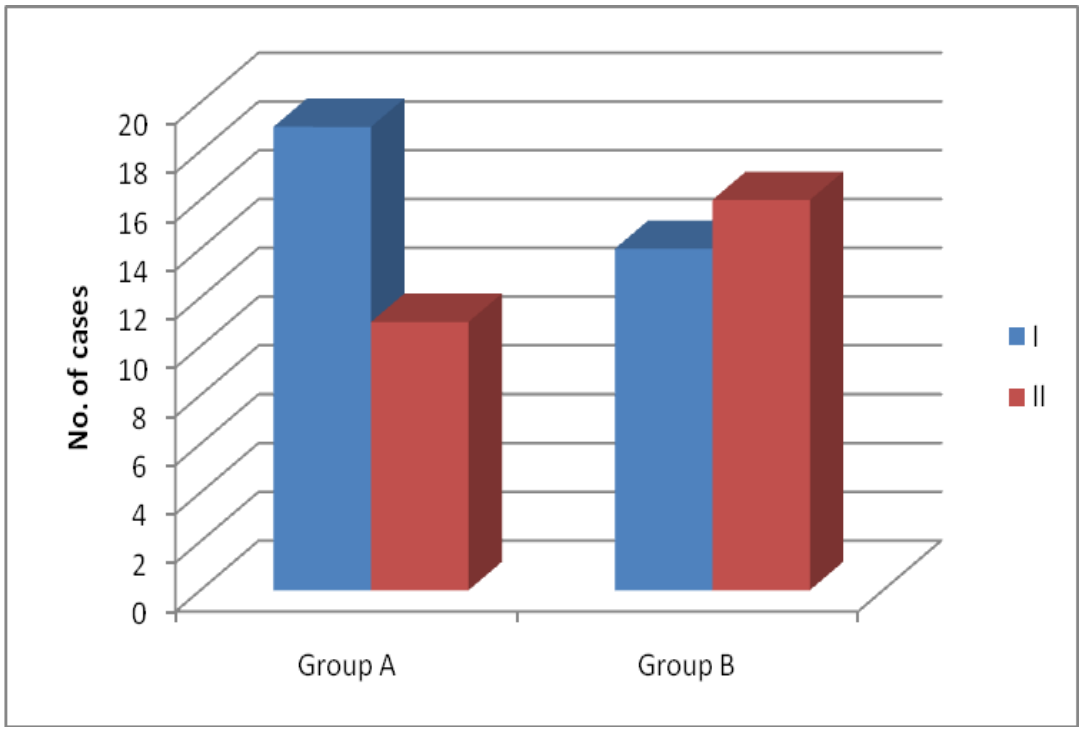

Figure 5. ASA physical status

Table 6. Trends in the postoperative mean heart rate (per minute)

HR(per minutes)	Group A		Group B		t	p-value
	Mean	SD	Mean	SD		
Immediately in the postoperative period	92.37	10.94	90.83	9.72	-0.574	0.568
1 hour	92.07	12.74	89.83	8.81	-0.790	0.433
2 hours	88.13	8.98	87.17	11.81	0.357	0.722
3 hours	86.83	8.07	82.77	11.24	1.610	0.113
4 hours	86.27	8.15	80.13	10.45	2.534	0.014
5 hours	84.47	8.14	77.73	8.78	3.080	0.003
6 hours	79.97	8.20	75.10	8.09	2.315	0.024
8 hours	78.47	8.36	72.80	7.86	2.705	0.009
10 hours	77.63	8.60	70.20	7.38	3.592	0.001
12 hours	76.83	9.15	71.23	7.22	2.632	0.011
16 hours	76.07	8.87	68.87	6.15	3.655	0.001
20 hours	75.67	8.99	67.57	6.23	4.055	0.001
24 hours	75.33	8.91	65.90	4.92	5.075	0.001

The mean baseline heart rate was 81.93 ± 11.62 min and 84.87 ± 12.77 min in groups A and B respectively. No statistically significant difference was observed in both groups with respect to mean heart rate (p value being 0.356). The mean heart rate at postoperative zero hour i.e. in the immediate postoperative period was 92.37 +/- 10.94 and 90.83 +/- 9.72 in groups A and B respectively, p value being 0.568. Thus the mean heart rate was statistically similar in the immediate postoperative period in the two groups. Thereafter, the mean heart rate at postoperative 1, 2, and 3 hours showed no statistically significant difference between the two groups. However, from 4 hours onwards till 24 hours, the heart rate was lower in group B than group A at all time intervals, the difference being statistically significant.

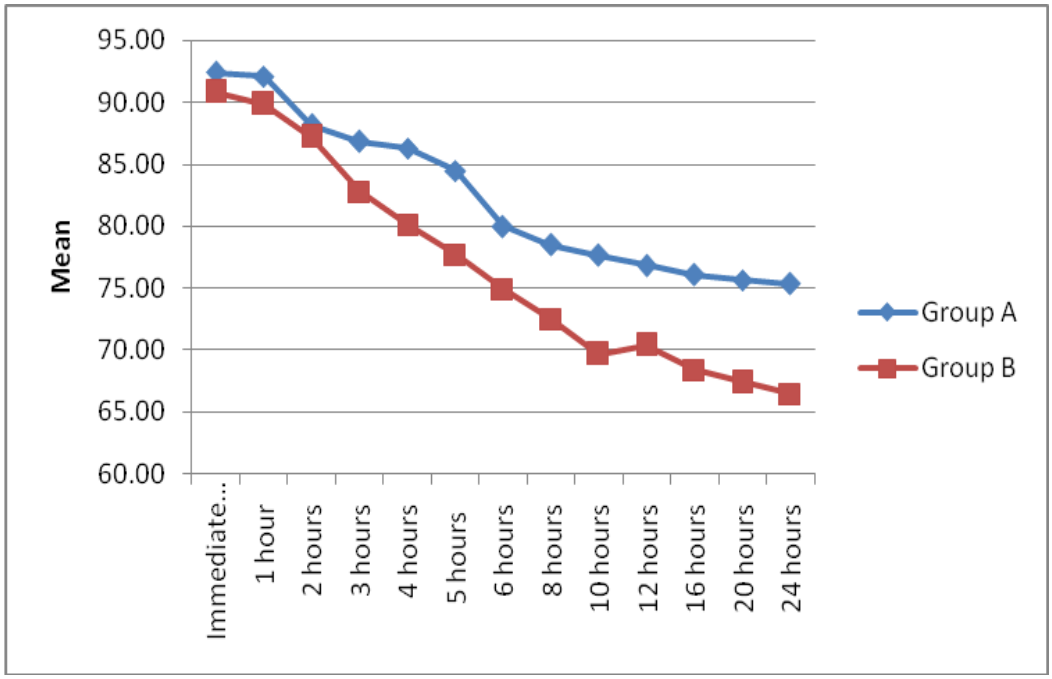

Figure 6. Trends in the postoperative mean heart rate (per minute)

Table 7. Trends in the postoperative mean systolic blood pressure (mm Hg)

SBP (mm Hg)	Group A		Group B		t	p-value
	Mean	SD	Mean	SD		
Immediately in the postoperative period	138.77	6.99	137.50	8.70	0.622	0.536
1 hour	137.57	6.91	134.77	9.03	1.349	0.183
2 hours	136.00	6.68	131.50	8.86	2.222	0.030
3 hours	135.00	6.67	128.57	8.83	3.182	0.002
4 hours	129.97	6.84	125.27	8.73	2.321	0.024
5 hours	128.10	6.38	122.67	8.68	2.763	0.008
6 hours	126.57	6.52	119.83	9.33	3.241	0.002
8 hours	126.63	6.37	117.33	10.22	4.230	0.001
10 hours	125.80	6.81	115.90	11.26	4.120	0.001
12 hours	124.33	6.57	115.80	11.47	3.535	0.001
16 hours	123.00	6.41	116.00	9.72	3.294	0.002
20 hours	122.70	5.91	117.00	7.35	3.310	0.002
24 hours	121.83	6.51	115.40	5.91	4.008	0.001

The mean baseline SBP was 127.87 ± 8.16 and 129.27 ± 8.85 mmHg in groups A and B respectively. No statistically significant difference in SBP was observed in both groups (p-value being 0.527). The mean SBP in the immediate postoperative period was 138.77 ± 6.99 mmHg and 137.5 ± 8.70 mmHg in groups A and B respectively, the p-value being 0.536. Thus there was no statistically significant difference observed in SBP in the immediate postoperative period amongst the two groups. The mean SBP at postoperative 1 hour between the two groups was also statistically comparable. However, from 2 hours onwards till 24 hours, the SBP was lower in group B than group A at all time intervals, the difference being statistically significant.

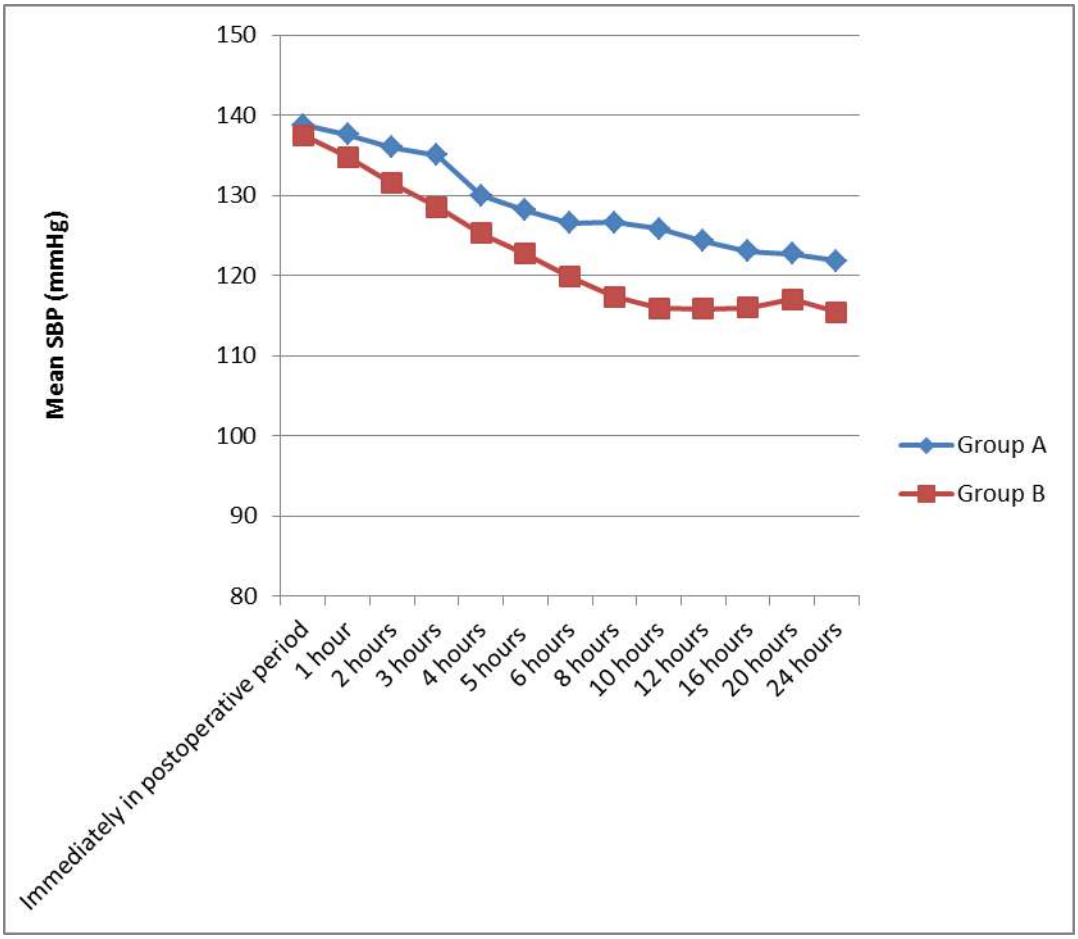

Figure 7. Trends in the postoperative mean systolic blood pressure (mm Hg)

Table 8. Trends in the postoperative mean diastolic blood pressure (mmHg)

Mean DBP (mm Hg)	Group A		Group B		t	p-value
	Mean	SD	Mean	SD		
Immediately in the postoperative period	83.27	7.62	85.57	7.80	-1.155	0.253
1 hour	80.43	8.49	83.83	8.51	-1.549	0.127
2 hours	78.83	9.03	81.87	8.55	-1.336	0.187
3 hours	78.70	8.98	79.80	8.23	-0.495	0.623
4 hours	77.97	8.48	77.67	8.20	0.139	0.890
5 hours	76.80	8.27	75.90	8.49	0.416	0.679
6 hours	76.73	7.93	74.53	8.08	1.065	0.291
8 hours	76.30	8.20	72.93	7.54	1.655	0.103
10 hours	75.10	8.37	70.87	8.02	2.001	0.050
12 hours	74.37	8.48	69.43	8.03	2.313	0.024
16 hours	73.77	8.30	69.50	6.94	2.159	0.035
20 hours	74.17	8.22	69.23	5.50	2.733	0.008
24 hours	73.73	8.35	68.10	5.35	3.110	0.003

The mean baseline DBP was 74.37 ± 8.95 mmHg and 77.87 ± 9.79 mmHg in groups A and B respectively. No statistically significant difference in DBP was observed in both groups (p value being 0.154). The mean DBP in immediate postoperative period was 83.27 ± 7.62 mm Hg and 85.57 ± 7.80 mm Hg in groups A and B respectively, p value being 0.253. Thus no statistically significant difference was observed in DBP in immediate postoperative period in the two groups. The two groups were statistically comparable in DBP at 1,2,3,4,5,6,8 hours. However, from 10 hours onwards till 24 hours, the DBP was lower in group B than group A at all time intervals, the difference being statistically significant.

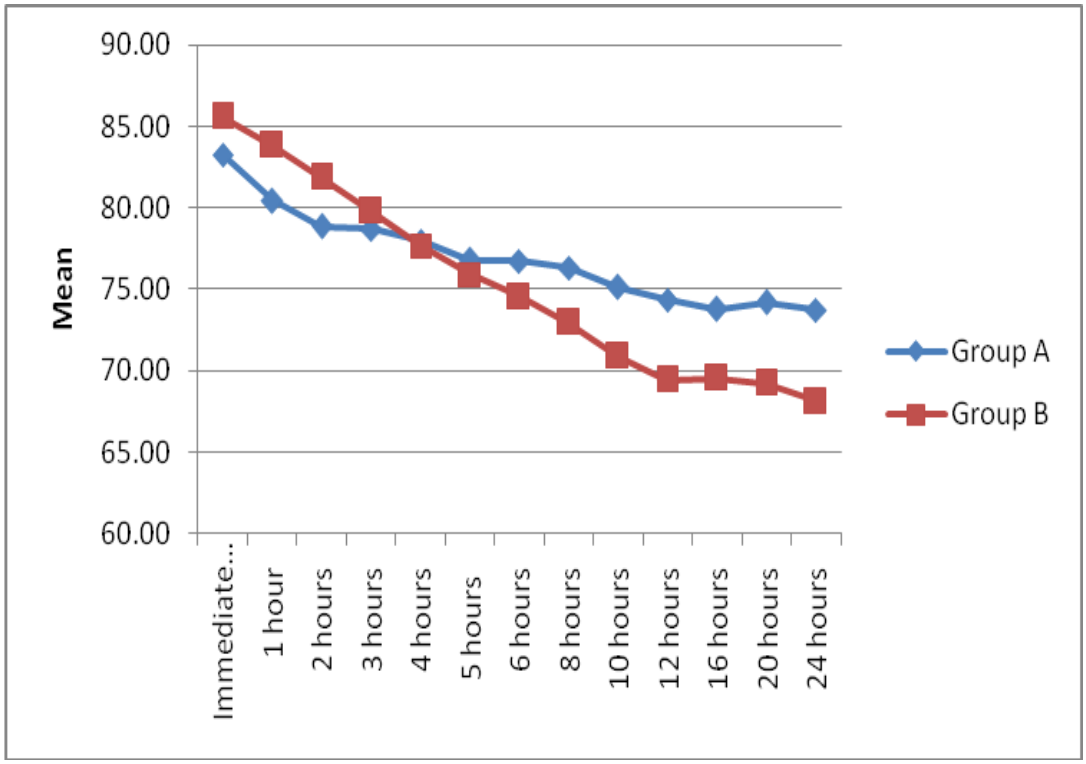

Figure 8. Trends in the postoperative mean diastolic blood pressure (mmHg)

Table 9. Trends in the Postoperative SpO2 (%)

SpO2 (%)	Group A		Group B		t	p-value
	Mean	SD	Mean	SD		
Immediate postoperative period	98.57	0.68	98.43	0.82	0.687	0.495
1 hour	98.10	1.03	98.07	0.94	0.131	0.896
2 hours	98.20	1.06	98.13	0.82	0.272	0.787
3 hours	98.13	1.04	97.90	0.92	0.918	0.362
4 hours	98.17	1.02	98.17	0.79	0.000	1.000
5 hours	98.07	1.01	98.27	0.94	-0.790	0.433
6 hours	97.93	1.05	98.27	1.05	-1.232	0.223
8 hours	98.07	1.01	98.30	1.02	-0.887	0.379
10 hours	98.07	1.01	98.17	0.95	-0.394	0.695
12 hours	98.17	1.02	98.07	0.83	0.417	0.678
16 hours	98.30	0.92	98.33	0.92	-0.141	0.889
20 hours	98.33	0.96	98.20	0.89	0.559	0.578
24 hours	98.40	1.07	98.27	1.05	0.488	0.628

Mean oxygen saturation immediately in postoperative period was 98.57 ± 0.68 % and 98.43 ± 0.82 % in group A and B respectively, which was statistically comparable (p value > 0.05). On intergroup comparison no falling or rising trend was seen. None of the patients in any of the groups had any fall in oxygen saturation which might have necessitated oxygen administration.

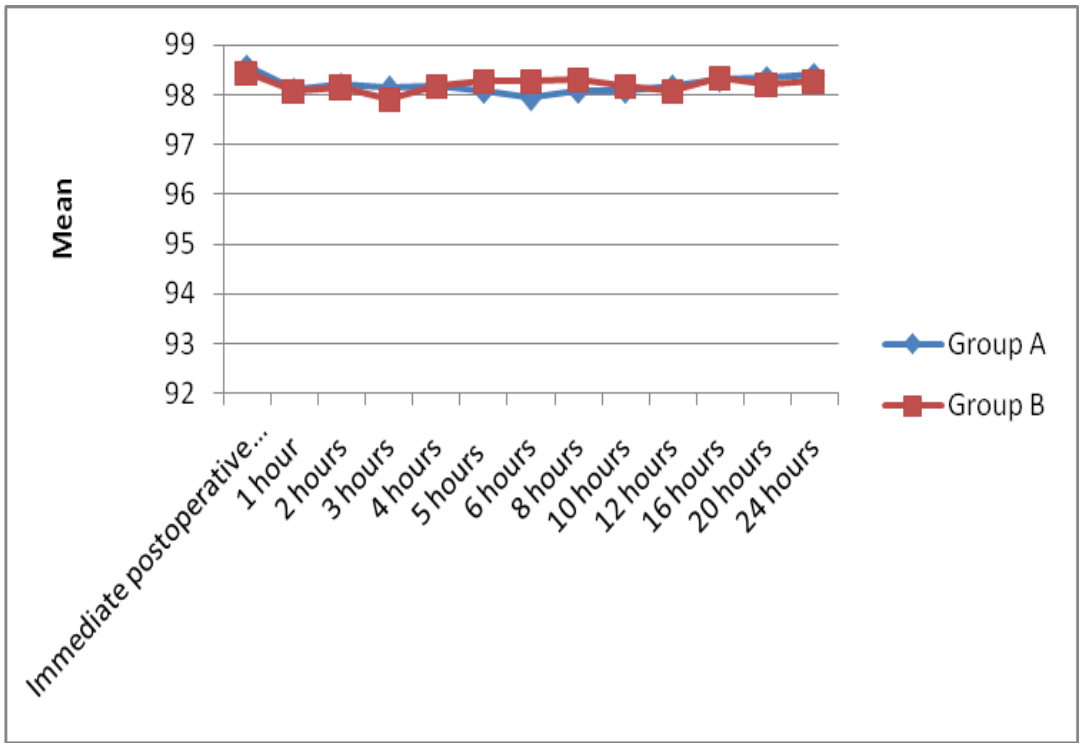

Figure 9. Trends in the Postoperative SpO2 (%)

Table 10. Trends in postoperative mean respiratory rate (breaths per minute)

Respiratory rate (breaths per minute)	Group A		Group B		t	p-value
	Mean	SD	Mean	SD		
Immediately in postoperative period	15.23	1.10	15.33	0.92	-0.381	0.705
1 hour	15.70	1.64	15.87	1.46	-0.416	0.679
2 hours	14.90	1.12	14.73	0.94	0.621	0.537
3 hours	15.10	1.06	14.87	0.94	0.902	0.371
4 hours	15.33	1.47	14.87	1.07	1.404	0.166
5 hours	15.60	1.30	15.27	0.98	1.120	0.267
6 hours	15.60	1.30	15.10	1.12	1.591	0.117
8 hours	16.10	1.30	15.90	1.18	0.624	0.535
10 hours	16.13	1.74	16.10	1.54	0.079	0.938
12 hours	15.53	1.36	15.30	1.02	0.752	0.455
16 hours	15.93	1.39	15.57	1.19	1.097	0.277
20 hours	16.07	1.70	15.57	1.65	1.154	0.253
24 hours	15.60	1.43	15.30	1.12	0.905	0.369

The mean respiratory rate immediately in the postoperative period was comparable in both the groups (p value > 0.05). The mean respiratory rate was normal in all patients at all time intervals. None of the patients required any respiratory assistance in the postoperative period.

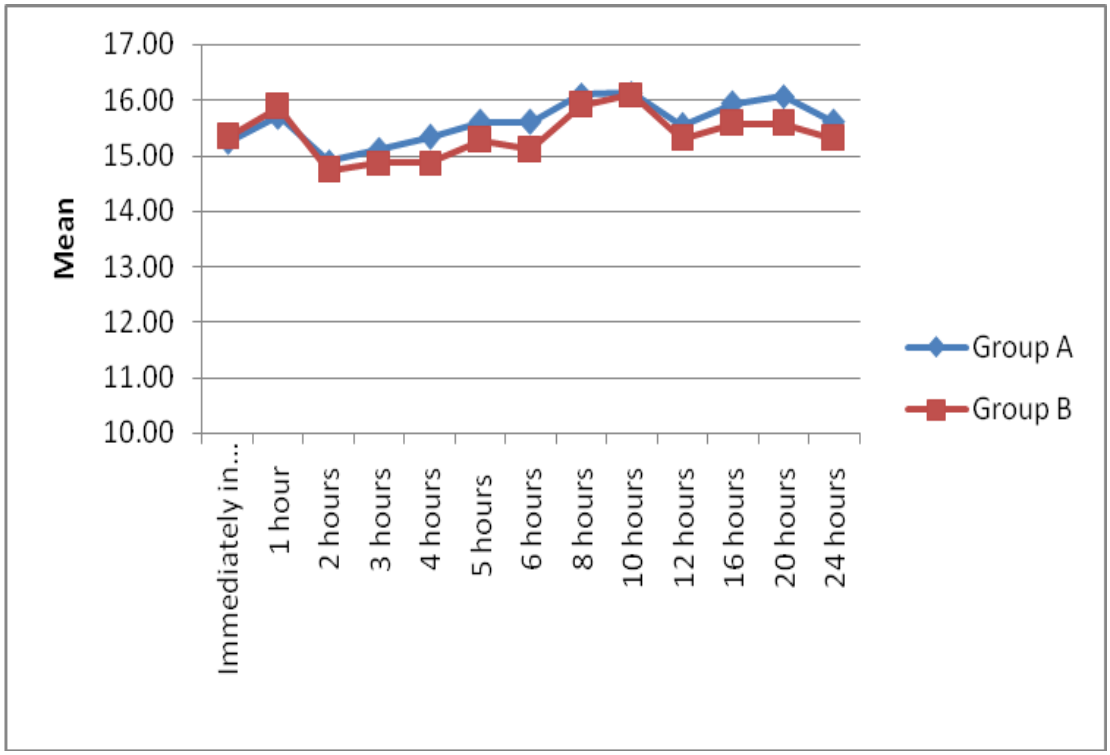

Figure 10. Trends in postoperative mean respiratory rate (breaths per minute)

Table 11. Trends in postoperative mean VAS score at rest at various time intervals

VAS at rest	Group A		Group B		Z	p-value
	Mean	SD	Mean	SD		
Immediately in postoperative period	0.80	0.48	0.77	0.43	0.282	0.779
1 hour	4.90	1.16	4.77	1.19	0.440	0.662
2 hours	2.93	0.25	2.93	0.25	0.000	1.000
3 hours	3.03	0.41	3.03	0.32	0.000	1.000
4 hours	3.67	0.80	3.63	0.81	0.160	0.873
5 hours	2.90	0.66	2.73	0.74	0.920	0.362
6 hours	2.93	0.45	2.80	0.55	1.027	0.309
8 hours	3.00	0.45	3.03	0.32	-0.328	0.744
10 hours	2.77	0.50	2.70	0.65	0.443	0.659
12 hours	2.73	0.52	2.77	0.43	-0.270	0.788
16 hours	3.03	0.18	3.00	0.00	1.000	0.321
20 hours	2.00	0.00	2.00	0.00	0.000	1.000
24 hours	1.00	0.00	1.00	0.00	0.000	1.000

The mean VAS score was 0.80 +/- 0.48 and 0.77 +/- 0.43 in groups A and B respectively in the immediate postoperative period. Thus both groups A and B were statistically comparable in terms of mean VAS scores in the immediate postoperative period. Thereafter, all patients in both the groups remained statistically comparable with respect to mean VAS score at all measurement time intervals till 24 hours.

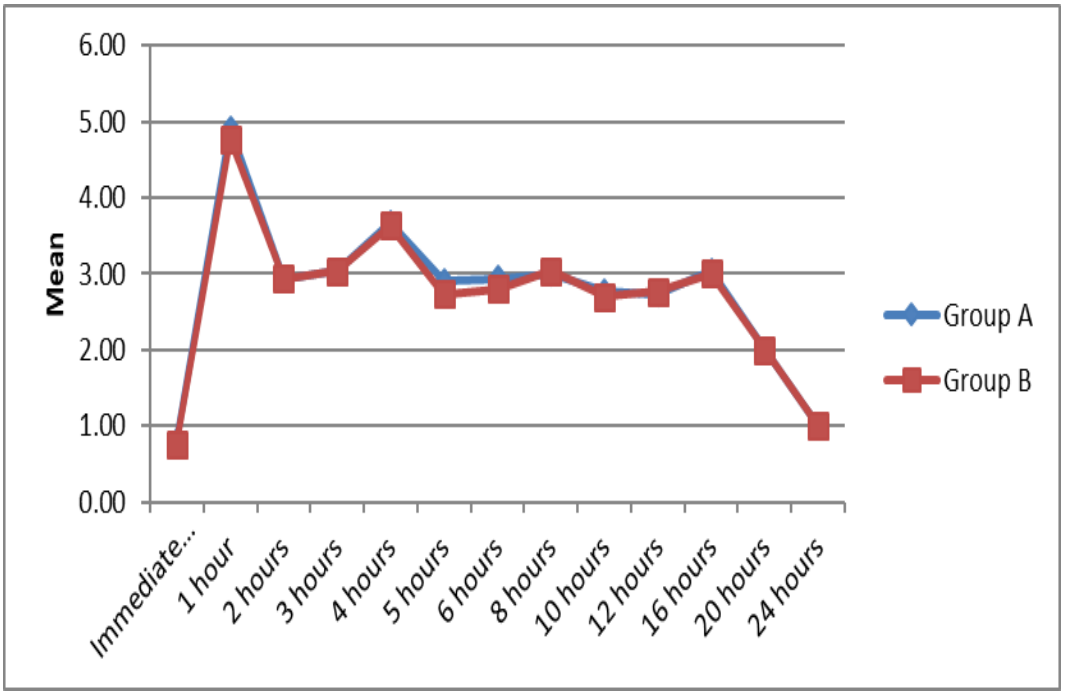

Figure 11. Trends in postoperative mean VAS score at rest at various time intervals

Table 12. The mean VAS score at time of administration of each rescue analgesic

VAS at time of administration of rescue analgesic	Group A		Group B		Z	p-value
	Mean	SD	Mean	SD		
1st dose	5.38	0.71	5.30	0.76	0.328	0.744
2nd dose	4.32	0.48	4.35	0.49	-0.213	0.832
3rd dose	4.00	0.00	4.00	0.00	0.000	1.000
4th dose	4.00	0.00	0.00	0.00	0.000	1.000

The mean VAS score at the time of administration of 1st, 2nd, 3rd and 4th rescue analgesic was statistically comparable in both the groups. (p value > 0.05).

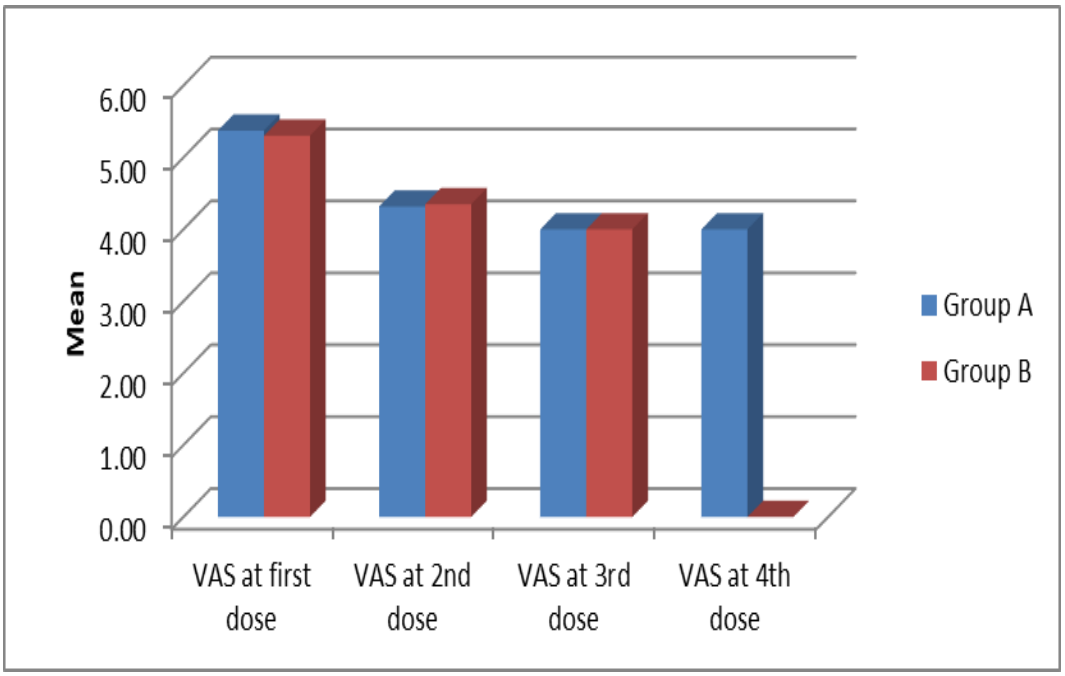

Figure 12. The mean VAS score at the time of administration of each rescue analgesic.

Table 13. Mean time to first rescue analgesic consumption (minutes)

	Group A		Group B		Z	p-value
	Mean	SD	Mean	SD		
Time of 1st dose of Rescue Analgesic (minutes)	67.13	3.55	75.83	2.33	-9.831	0.001

Mean time of first rescue analgesic consumption was 67.13 ± 3.55 min and 75.83 ± 2.33 min for group A and group B respectively, which was statistically significant (p value <0.05) . Thus patients in group B were administered first rescue analgesia later than patients in group A.

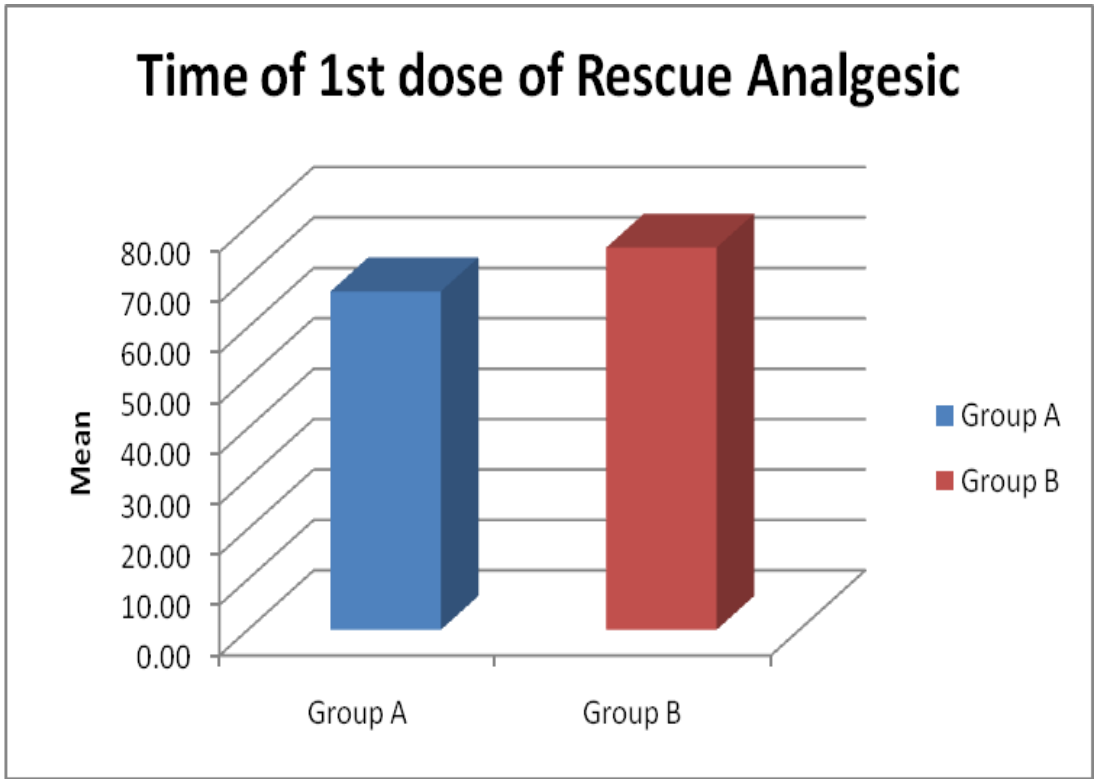

Figure 13. Mean time to first rescue analgesic consumption (minutes)

Table 14. Mean time to second rescue analgesic consumption (minutes)

	Group A		Group B		Z	p-value
	Mean	SD	Mean	SD		
Time of 2nd dose of Rescue Analgesic (minutes)	262.05	44.99	291.70	38.17	-2.291	0.027

Patients in group A were administered a second dose of rescue analgesia at 262.05 ± 44.99 minutes whereas, those in group B were administered a second dose of rescue analgesia at 291.70 ± 38.17 minutes, which was statistically significant (p value < 0.05). Thus the patients in group B had a longer time interval to second dose of rescue analgesia consumption than those in group A.

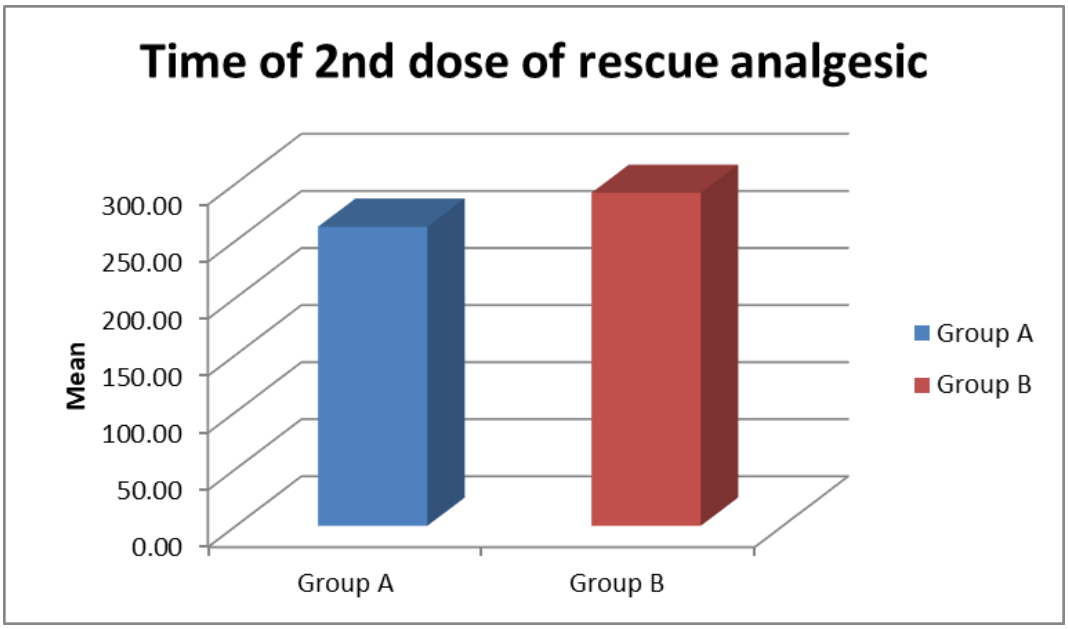

Figure 14. Mean time to second rescue analgesic consumption (minutes)

Table 15. Total rescue analgesic (tramadol) consumption in 24 hours (mg)

	Group A		Group B		Z	p-value
	Mean	SD	Mean	SD		
Total rescue analgesic(tramadol) consumption in 24 hours (mg)	85.00	55.94	80.00	53.50	0.354	0.725

Patients in group A consumed a mean total rescue analgesic (tramadol) dose of 85.00 ± 55.94 mg in 24 hours compared to 80.00 ± 53.50 mg in patients of group B. Thus mean rescue analgesic (tramadol) consumption in 24 hours was statistically comparable in both the groups (p value > 0.05)

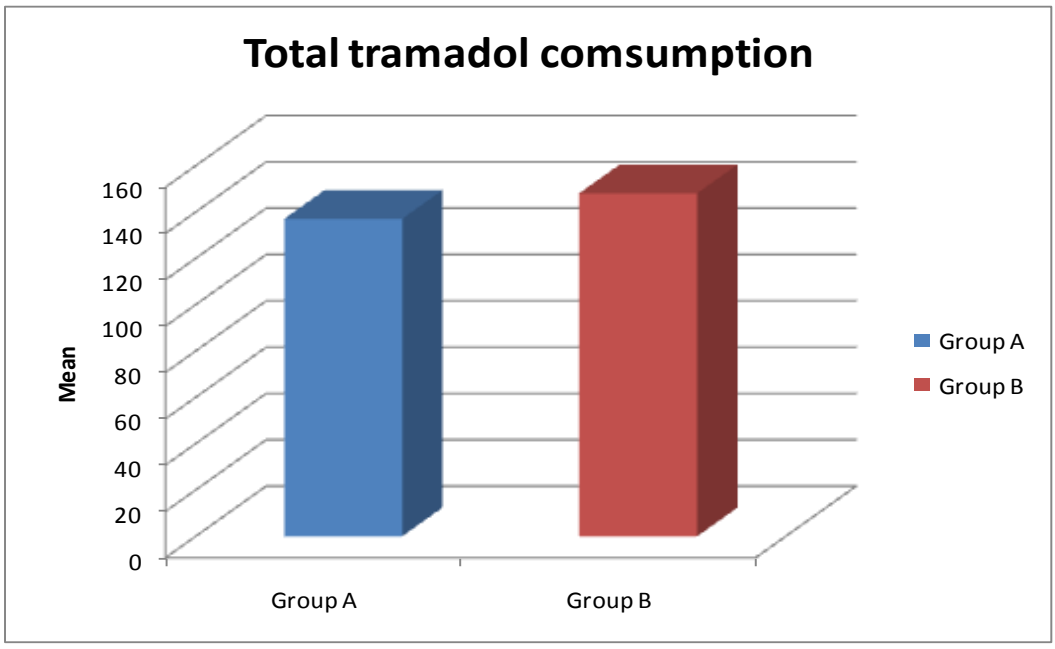

Figure 15. Total rescue analgesic (tramadol) consumption in 24 hours (mg)

Table 16. Number of times rescue analgesic given

		Group A	Group B	Total	Chi-square value	p-value
Total number of times rescue analgesic given	No dose	7	7	14	0.651	0.957
	once	1	2	3	0.351	0.554
	twice	18	16	34	0.272	0.602
	thrice	2	3	5	0.218	0.641
	4 times	2	2	4	<0.001	0.001
Total		30	30	60		

In group B, 7 patients did not require any rescue analgesic over 24 hours postoperative period, 2 required it once and 16 received it twice, 3 received it thrice while 2 received it 4 times. In group A, 7 patients did not require any rescue analgesic, 1 patient received it once, 18 received rescue analgesic twice, 2 patients received it thrice while 2 patients received it four times. Thus, group B patients required rescue analgesic for statistically comparable times as group A patients.(p value > 0.05)

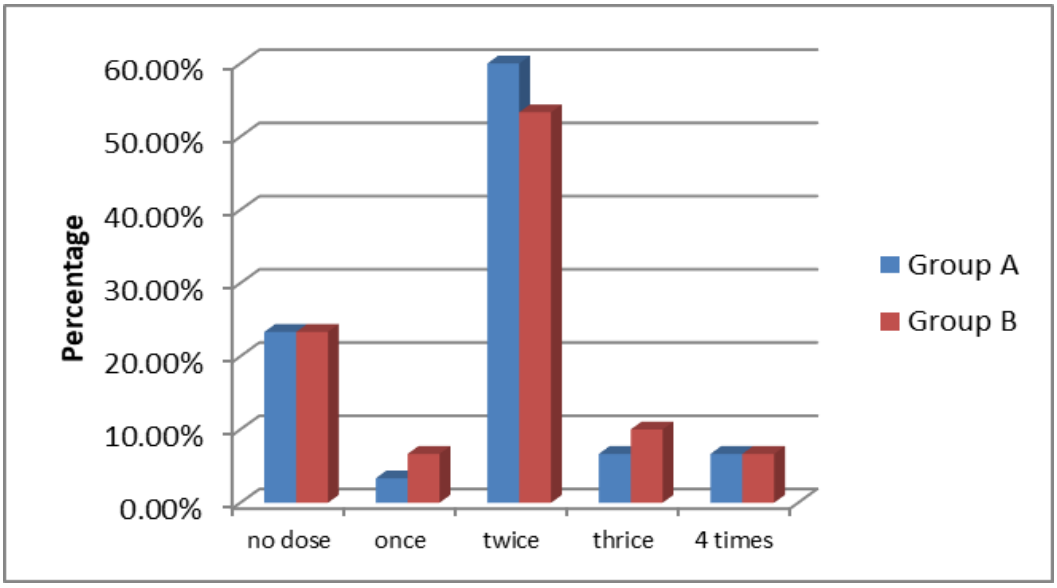

Figure 16. Number of times rescue analgesic given

Table 17. Mean Ramsay sedation score

Mean Ramsay sedation score	Group A		Group B		Z	p-value
	Mean	SD	Mean	SD		
Immediate postoperative period	2.07	0.25	3.00	0.00	-20.149	0.000
1 hour	2.03	0.18	3.00	0.00	-29.000	0.000
2 hours	2.03	0.18	3.00	0.00	-29.000	0.000
3 hours	2.03	0.18	3.00	0.00	-29.000	0.000
4 hours	2.07	0.25	2.90	0.31	-11.502	0.000
5 hours	2.03	0.18	2.70	0.47	-7.295	0.000
6 hours	2.03	0.18	2.40	0.50	-3.785	0.000
8 hours	2.00	0.00	2.13	0.35	-2.112	0.039
10 hours	2.00	0.00	2.03	0.18	-1.000	0.321
12 hours	2.00	0.00	2.00	0.00	0.000	1.000
16 hours	2.00	0.00	2.00	0.00	0.000	1.000
20 hours	2.00	0.00	2.00	0.00	0.000	1.000
24 hours	2.00	0.00	1.97	0.18	1.000	0.321

Mean Ramsay sedation score was higher in group B patients than group A patients from immediate postoperative period onwards till 8 hours, at all time intervals, the difference being statistically significant (p value < 0.05). Thus group B patients were more sedated than group A patients till postoperative 8 hours. Thereafter from postoperative 10 hours onwards, till 24 hours, sedation score was statistically comparable in both groups A and B (p value > 0.05). However, none of the patients in any of the groups had mean ramsay sedation score of 5 or more.

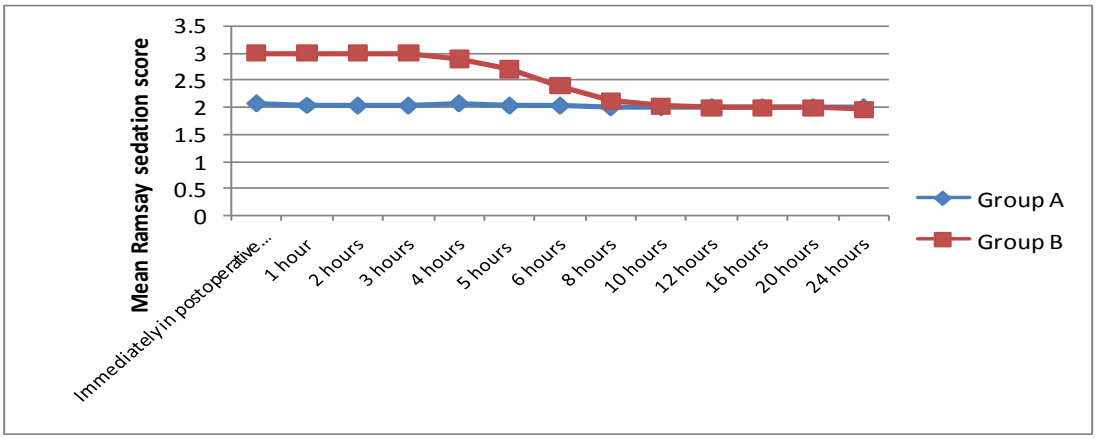

Figure 17. Mean Ramsay sedation score

Table 18. Incidence of postoperative adverse effects (%)

						Total	Chi-square value	p-value
		Group A	Group A	Group B	Group B			
Incidence of postoperative adverse effects (%)								
	Bradycardia + Hypotension	0	0.00%	2	6.67%	2	2.069	0.150
	Bradycardia	0	0.00%	7	23.33%	7	7.925	0.005
	Hypotension	0	0.00%	8	26.67%	8	9.687	0.039
	Nausea	3	10.00%	0	0.00%	3	3.158	0.237
Total		30	100.00%	30	100.00%	60		

The incidence of bradycardia was 23.33% in group B, while in group A none of the patients had bradycardia. Therefore, upon intergroup comparison, the difference of incidence of bradycardia was statistically significant (p value < 0.05).

The incidence of hypotension was 26.67% in group B, while in group A, hypotension did not occur in any patient. However, the statistical difference in the incidence of hypotension between the two groups was not significant. (p value > 0.05).

The incidence of bradycardia and hypotension was 6.67 % in group B while none of the patients in group A had bradycardia and hypotension. The difference in incidence of bradycardia and hypotension was statistically comparable between the two groups.

The incidence of nausea was 10% in group A, while in group B, the incidence of postoperative nausea was negligible. However, the incidence of nausea was statistically comparable in group B as compared to group A (p value <0.05).

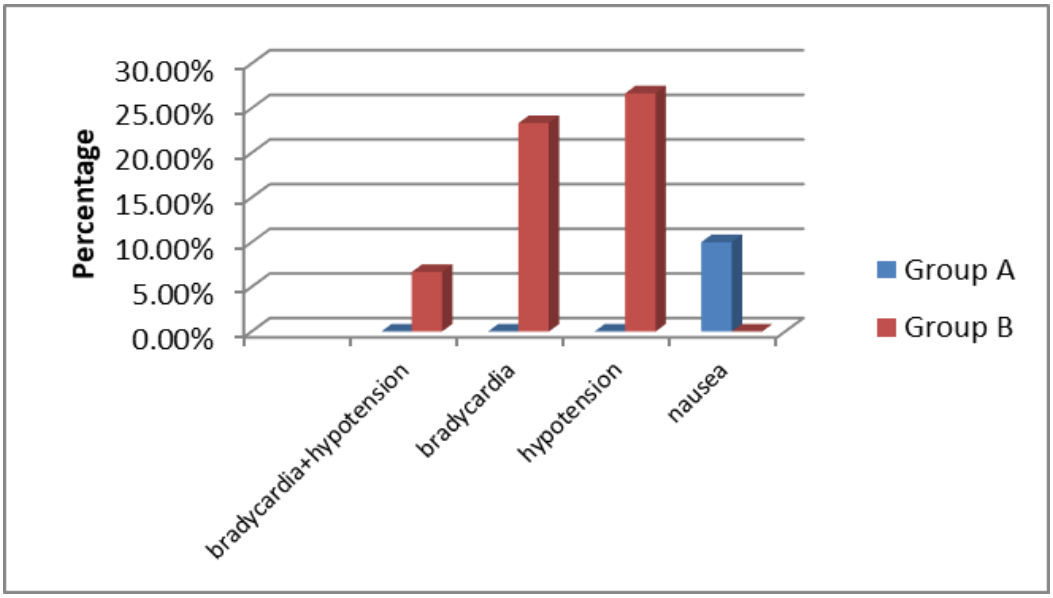

Figure 18. Incidence of postoperative adverse effects (%)

Table 19. Mean atropine bolus administered

	Group A		Group B		Total	Chi-square value	p-value
	Number of cases	%age	Number of cases	%age			
Number of patients requiring Atropine	0	0.00%	9	30.00%	9	10.588	0.002
Number of Atropine bolus given	0	0.00	12	0.00	12	15.000	0.001

The mean number of cases in which atropine bolus was given was higher in group B (30 %) than in group A (0%). On intergroup comparison, the difference was statistically significant. (p-value > 0.05). The total no. of atropine boluses given was 12 in group B and none of the patients in group A needed any atropine bolus. On intergroup comparison, the difference was statistically significant. (p-value > 0.05). The mean dose of atropine administered in Group B was 7.2 mg while none of the patients in group A received atropine.

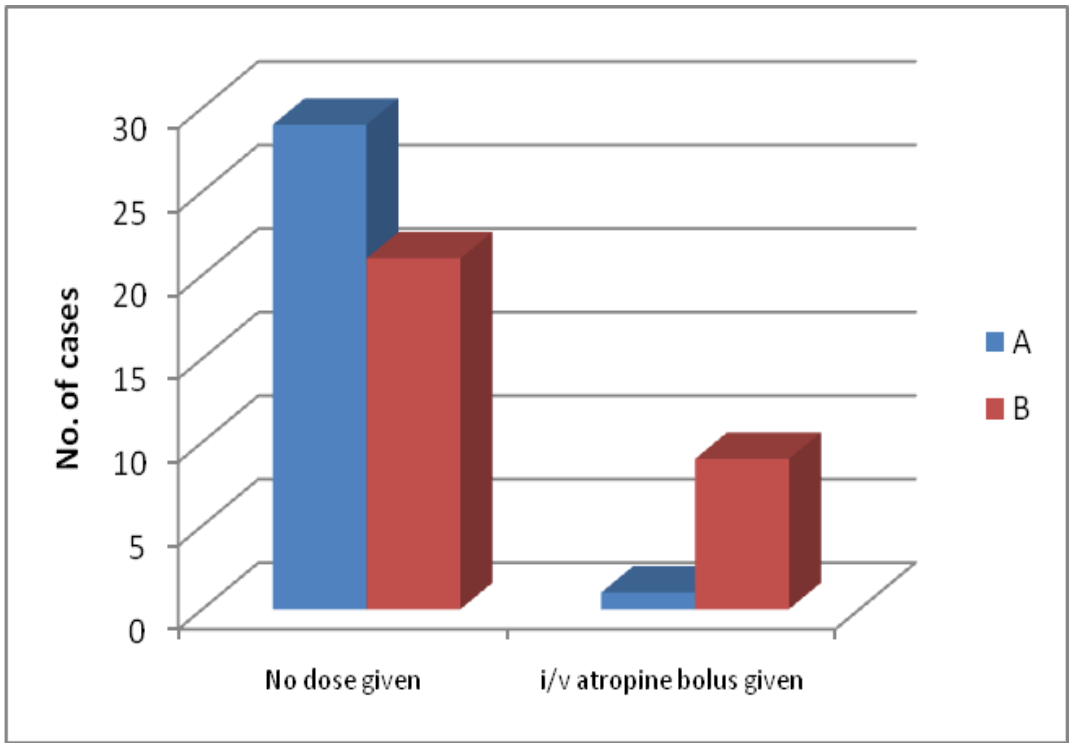

Figure 19. Mean atropine bolus administered.

Table 20. Mean ephedrine bolus administered.

		Group A		Group B		Total	Chi-square value	p-value
	Number of patients	%age						
Number of patients requiring ephedrine	0	0.00%	10	10	33.33%	12.000	0.001	0.0001
Number of ephedrine bolus given	0	0.00	10	10	0.00	12.000	0.001	

The mean number of cases in which ephedrine bolus was given was higher in group B (33.33%) than in group A(0 %). On intergroup comparison, the difference was statistically significant(p value < 0.05). In group B 10 patients needed ephedrine bolus while in group A, none of the patients needed ephedrine bolus. On intergroup comparison the difference was statistically significant. (p value < 0.05). Total dose of ephedrine administered in group B was 60 mg while none of the patients received ephedrine bolus.

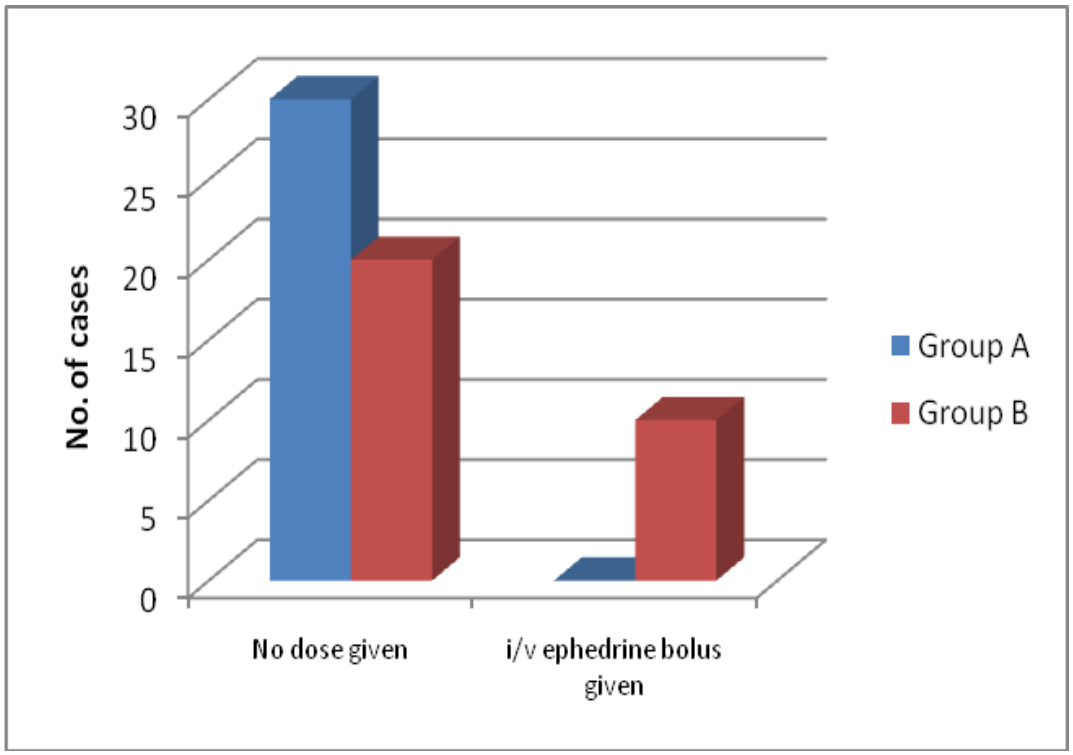

Figure 20. Mean ephedrine bolus administered.

DISCUSSION

Pain after total laparoscopic hysterectomy if untreated or poorly managed can lead to long-term consequences like chronic pain etc.[3,4] As conventional analgesic regimens are fraught with adverse effects, there has been a quest to identify analgesic infusion regimens to improve analgesia and reduce unwanted effects.

Various studies have been conducted on intravenous administration of alpha 2 agonists like dexmedetomidine, and analgesic adjuvants like lignocaine in different surgeries. The efficacy of their intraoperative and perioperative infusions, along with their safety profile has been evaluated. However, studies to compare the efficacy of perioperative dexmedetomidine and lignocaine infusions for postoperative analgesia in total laparoscopic hysterectomy, have been few.

In our study, sixty patients undergoing total laparoscopic hysterectomy, belonging to ASA grade I or II were selected and randomly categorized into two groups A and B of 30 patients each. They were administered the study drugs intravenously, each diluted to make a volume of 20 ml, given over 10 min as a loading dose in pre-induction period, and then diluted to make a volume of 50 ml, given as maintenance dose during the entire surgical procedure and the first 24 hours after surgery.

Group A- patients were treated with lignocaine 1.5 mg/kg loading dose followed by 1mg/kg/hr maintenance dose.

Group B- Patients were treated with dexdexmedetomidine 1 mcg/kg/hr loading dose followed by 0.6 mcg/kg/hr maintainence dose.

The above-mentioned doses of study drugs were decided based on the available literature. Abd El Megid et al administered a loading dose of dexmedetomidine 1mcg/kg/hr followed by a maintenance dose infusion of 0.6mcg/kg/hr for 24 hours, in patients undergoing uvulopharyngoplasty. [51] The authors found this dose to be effective in postoperative pain relief with

minimal side effects. Rabie et al compared intraoperative dexmedetomidine infusions of 0.4 mcg/kg/hr and 0.6 mcg/kg/hr in patients undergoing laparoscopic cholecystectomy and found that analgesic efficacy of 0.6 mcg/kg/hr infusion was more than 0.4mcg/kg/hr infusion.[55] Dailey et al administered a higher dose dexmedetomidine infusion of 0.7 mcg/kg/hr for >24 hours in management of alchohol withdrawal and found that 50% of these patients suffered significant adverse effects like hypotension.[56] Castillo et al administered dexmedetomidine infusion 0.2-1.5 mcg/kg/hr with a maximum average dose of 1mcg/kg/hr in critically ill patients and found that this dose caused significant adverse effects like bradycardia and hypotension in 50 % of the patients.[57] Therefore we chose a bolus dose of 1mg/kg followed by a maintenance infusion of 0.6 mcg/kg/hr that was effective in providing analgesia and also had lesser side effects than higher doses. The recommended dose range of intravenous dexmedetomidine is 0.2 to 0.7 mcg/kg/hr for no more than 24 hours.[42]

Ho et al used intravenous lignocaine in a loading dose of 1.5 mg/kg and a maintenance infusion of 1mg/kg/hr in patients undergoing open colorectal surgery and found this dose to be associated with very less adverse effects. [68] Anis et al in a study on laparoscopic gynecologic surgery, found intraoperative lignocaine bolus of 1.5 mg/kg to be effective in reducing postoperative pain scores. This dose also resulted in minimal hemodynamic disturbances.[81] Based on evidence from various studies, Epie et al, concluded that the most widely reported and clinically effective dose range of intravenous lignocaine appears to be from 1 to 2 mg/kg/hr.[64] At this dose range, it usually results in plasma concentrations that remain below 5 mcg/ml (dose at which signs of toxicity begin to appear). The use of lignocaine infusion for 24 hours in this dose range also shows a significant analgesic effect and an opioid-sparing effect.[64] Therefore we used lignocaine in a dose of 1.5 mg/kg bolus followed by a maintenance infusion of 1 mg/kg/hr.

The patients in both the groups were comparable with respect to age, BMI and preoperative values of clinical variables(SBP, DBP, MAP, RR, HR and SPO_2). In the postoperative period, patients were assessed for 24 hours based on hemodynamic parameters, visual analog scale pain score, the total opioid consumption, time to first and second rescue analgesia, adverse effects, number of boluses, and dose given for the treatment of adverse effects.

In our study, the baseline hemodynamic parameters in both the groups were similar. In the postoperative study period, statistically significant lower values of heart rate and BP were observed in group B as compared to group A. Our results are in concordance to those of Xu et al , who compared lignocaine (1.5 mg/kg bolus dose and 1.5 mg/kg/hr maintenance infusion) and dexmedetomidine (0.5 mcg/kg bolus dose and 0.4 mcg/kg/hr maintenance infusion) administered intraoperatively.[80] They found statistically significant drop in HR and BP recordings in dexmedetomidine group than lignocaine group. In contrast, Priye et al , administered dexmedetomidine (0.4 mcg/kg/hr) infusion , without a loading dose , and continued it postoperatively for 12 hours.[52] They found no difference in HR and BP as compared to saline group. A possible explanation for difference in our findings could be that we used a bolus dose (1 mcg/kg) and a higher maintenance infusion dose of dexmedetomidine (0.6 mcg/kg/hr) in our study as compared to Priye et al. Abd El Megid et al administered dexmedetomidine (1mcg/kg bolus dose and 0.6 mcg/kg/hr maintenance dose for 24 hours) in obese patients undergoing uvulopharyngoplasty and observed no difference in HR and BP as compared to saline group.[51] A possible explanation for difference with our findings, despite similar doses, is the difference in nature of surgery and different patient population. Most studies on dexmedetomidine have reported decrease in heart rate and BP following infusion of dexmedetomidine.[89]

The possible mechanism for dexmedetomidine induced reduction in heart rate and MAP is the sympathetic inhibition of the medullary vasomotor center upon activation of alpha 2 receptors causing a dose-dependent reduction in the levels of plasma catecholamines, bradycardia, and hypotension.[42-46]

In our study, none of the patients in any of the groups had any fall in oxygen saturation which might have necessitated oxygen administration, at any time interval in the postoperative period. The mean respiratory rate was normal in all patients in both the groups at all time intervals. None of the patients required any respiratory assistance in the postoperative period. This finding is important because this indicates safety of dexmedetomidine infusion administration for 24 hours. Similar findings were observed by Abd El Megid at al and Ho et al who used dexmedetomidine and lignocaine infusions in their studies in the same dose and duration as used by us.[51,68] Rekatsina et al compared lignocaine (bolus: 1.5 mg/kg, infusion: 1.5 mg/kg/ h)and dexmedetomidine(bolus: 0.6 µg/kg, infusion: 0.6 µg/kg/h) in patients undergoing abdominal gynecological surgeries, and similar to our observations they found no variation in oxygen saturation and respiratory rate in their patients.[77] Dexmedetomidine is known to cause natural sleep like state without causing any respiratory depression. [89]

In our study, the baseline VAS scores in both groups were similar. During the study period, at various time intervals of 1, 2, 3, 4, 5, 6, 8, 10,12, 20, and 24 hours postoperatively, the VAS scores in both the groups were statistically similar. This could be because, either dexmedetomidine and lignocaine infusions are equi-efficacious in mitigating post-operative pain or the other plausible explanation could be that all patients were being monitored continuously and at any time interval, if they complained of pain, rescue analgesia was promptly administered.

Cho et al compared intraoperative lignocaine in a bolus dose of 1.5 mg/kg followed by a maintenance infusion of 2 mg/kg/hr versus intraoperative dexmedetomidine 1 mcg/kg bolus dose and 0.4 mcg/kg/hr maintenance infusion. They found that VAS scores were similar during the first 24 hours after laparoscopic cholecystectomy among both groups.[79]

Abd El Megid et al administered similar doses of dexmedetomidine for the same duration (24 hours) as used by us, and they observed that postoperative VAS scores were significantly better in dexmedetomidine group than saline group in first 2 hours after which the pain scores were similar in both the groups. [51]. The observed difference from our findings could be because of different nature of surgery, selection of obese patients and administration of dexmedetomidine bolus 30 min before end of surgery by Abd El Megid et al. Ho et al used lignocaine infusion in the same bolus and maintenance dose as used by us and observed no effect on postoperative VAS scores. [68]

In contrast, Anis et al compared intraoperative infusions of lignocaine in a dose of 2 mg/kg/hr and dexmedetomidine in a dose of 0.4 mcg/kg/hr in patients undergoing diagnostic laparoscopic gynaecological procedures and observed that postoperative pain scores were better in the lignocaine group than dexmedetomidine group for the initial postoperative period of 2 hours after which the pain scores were comparable in both the groups.[81] A possible explanation for the difference in findings could be that Anis et al used higher dose of lignocaine infusion and a lower dose of dexmedetomidine infusion in their study and the infusion was continued in intraoperative period only as compared to postoperative infusion of dexmedetomidine and lignocaine used in our study.

In contrast, Mohammed et al used a lignocaine infusion dose of 0.5 mg/kg/hr and dexmedetomidine infusion dose of 0.5 mcg/kg/hr in patients undergoing lumbar fixation surgery and reported that postoperative VAS score was significantly better in the dexmedetomidine group than

lignocaine group at 2,4,6,9,12,18 and 24 hours.[83] This difference could be explained by the fact that the lignocaine used in this study was much less than has been used in our study. Both lignocaine and dexmedetomidine have been demonstrated to have dose dependant analgesic effects in proportion to their concentrations.[58,65]

Mechanisms explaining the analgesic effect of intravenous lidocaine are- suppression of neuronal excitability (in myelinated A-ä and unmyelinated C fibers), suppression of central sensitization, inhibition of spinal visceromotor neurons, anti-inflammatory effects, blockade of nerve conduction, and decreased N-methyl-d-aspartate receptor activity, which plays a major role in postoperative hyperalgesia.[59-63] The receptors located in the locus ceruleus and the dorsal horn of spinal cord are implicated in the analgesic action of Dexmedetomidine. Dexmedetomidine also reduces transmission of the nociceptive signal by activating alpha 2-AR in the spinal cord.[42-46]

In our study, the mean opioid (tramadol) consumption in 24 hours in Group A was 85 ± 55.94 mg compared to 80 ± 53.50 mg in group B. Thus there was no statistically significant difference in the mean total opioid consumption between the two groups (p-value 0.725). Abd El Megid et al also reported lower opioid consumption than saline group in their study where they used a bolus dose of 1 mcg/kg and maximum dose of 0.6 mcg/kg/hr.[51] Ho et al , used lignocaine in a bolus dose of 1 mg/kg/hr and continued infusion for 24 hours and found similar opioid consumption as compared to saline in first 24 hours and reduced opioid consumption from postoperative 24 hours onwards.[68] This could be because they administered the drug in open surgery which has propensity to cause more pain than laparoscopic surgery.

Cho et al and Kumari et al, in their individual studies on patients undergoing laparoscopic cholecystectomy, also observed that opioid consumption was similar in patients receiving lignocaine (1.5 mg/kg bolus

dose followed by 2 mg/kg/hr maintenance infusion) and dexmedetomidine (1 mcg/kg bolus dose followed by 0.4 mcg/kg/hr maintenance infusion).[79, 82] Andjelkovic et al compared infusion of lignocaine 1.5 mg/kg/hr and dexmedetomidine 0.5mcg/kg/hr (without a loading dose) in patients undergoing laparoscopic intestinal resection and found that both the drugs resulted in similar reduction in opioid consumption in the postoperative period.[84] Our results are also in concordance with those of Anis et al, who observed that dexmedetomidine infusion at the rate of 0.4 mcg/kg/hr resulted in statistically comparable opioid sparing effect as would an infusion of lignocaine in a dose of infusion dose of 2 mg/kg/hr, for patients undergoing diagnostic laparoscopic gynaecological surgery.[81]

Our results however, are in contrast to those of Mohammed et al, who observed that lignocaine infusion had lesser opioid sparing effects as compared to dexmedetomidine infusion. The difference in results could be due to the fact that lignocaine was used in a much reduced dose by Mohammed et al (0.5 mg/kg/hr) as compared to the present study.[83] Another study by Rekatsina et al had different observations from our findings.[77] In their study, dexmedetomidine (bolus: 0.6 µg/kg, infusion: 0.6 µg/kg/h) and lidocaine (bolus: 1.5 mg/kg, infusion: 1.5 mg/kg/ h) were compared in abdominal gynecological surgeries, and lignocaine showed significant opioid-sparing as compared to dexmedetomidine. A possible explanation for the difference in their observations from our study could be because of a lower maintenance dose of lignocaine used in our study.

Our study showed a statistically significantly longer time to first postoperative analgesic demand in the dexmedetomidine group than the lignocaine group. Time to first rescue analgesic consumption was more in Group B (75.83 ± 2.33minutes) than Group A (67.13 ± 3.55 minutes). This observation is analogous to findings by Abd El Megid et al, who used dexmedetomidine in the same dose and duration as used in our study. They observed that time to first postoperative analgesic was prolonged in

dexmedetomidine group than saline group.[51] Menshawi et al who administered dexmedetomidine (bolus dose 1 mcg/kg; maintenance infusion 0.5 mcg/kg/hr) and lignocaine (bolus dose 1.5 mg/kg and maintenance infusion 2 mg/kg/hr) in patients undergoing elective abdominal surgery.[78] They observed that dexmedetomidine had a longer time to first postoperative analgesic demand than lignocaine. Also supporting our findings, was the study by Mohammed et al, who in their study using 0.5 mcg/kg/hr dose of dexmedetomidine and 0.5 mg/kg/hr dose of lignocaine also observed that time to first analgesic demand is higher in the dexmedetomidine group than lignocaine group.[83]

Patients in group B had a mean Ramsay sedation score of 3 compared to 2.07 in group A in the immediate postoperative period. For initial 8 hours, patients in group B had a higher Ramsay sedation score compared to patients in group A, the results being statistically significant, with no difference in sedation scores thereafter till 24 hours. One plausible explanation for longer time to first rescue analgesia consumption could be higher Ramsay sedation scores in group B.

Dexmedetomidine induces sedation while maintaining rousability, and without causing respiratory depression. Thus, this effect resembles physiological sleep. This effect is mediated by the modulation of the descending noradrenergic pathway, originating from locus ceruleus of the brain stem.[42-46] Lignocaine also is reported to cause deep sedation when used in very large doses.[65] Our study observed that patients in the dexmedetomidine group were sedated, but arousable with verbal or physical stimuli, without a need to decrease or stop the dexmedetomidine infusion. While those in the lignocaine group did not have any sedation. In concordance with our findings, Cho et al observed that the dexmedetomidine group had a higher sedation score in the immediate postoperative period than the lignocaine group.[79] Our findings were also comparable to Anis et al, who observed in patients undergoing

laparoscopic gynecological surgeries, the dexmedetomidine group had a higher sedation score in the immediate postoperative period, lasting up to 12 hours.).[81] In contrast to our findings, Abd El Megid et al in their study, did not observe any difference in sedation scores in dexmedetomidine group as compared to saline group. [51] Also, in contrast Szmuck et al , in their study on the effect of lignocaine on pain perception, observed that high dose lignocaine infusion (5mg/kg/hr) resulted in deep sedation in all patients.[65] However, we did not observe the sedative effect of lignocaine, possibly because the dose of lignocaine used by us (1mg/kg/hr) was lesser than used by Szmuck et al.

In our study, in the dexmedetomidine group,9 patients had bradycardia and 10 patients had hypotension, while in the lignocaine group none of the patients had bradycardia or hypotension. The difference in observations between the two groups was statistically significant. For each episode of bradycardia, atropine 0.6 mg IV was administered. Out of 9 patients, 3 patients required bolus dose of atropine at two time intervals. The hypotensive episodes were transient and MAP returned to within 25% of the baseline values within 5 min of administration of a fluid bolus and administration of 6mg ephedrine IV.

Several studies have similar findings to our observations. Cho et al used 1.5 mg/kg lignocaine bolus followed by 2 mg/kg/hr maintenance infusion versus 1mcg/kg dexmedetomidine bolus followed by 0.4 mcg/kg/hr maintenance infusion, and observed that heart rate in the dexmedetomidine group was significantly lower in the dexmedetomidine group than lignocaine group at all times till discharge from PACU. [79]Similar findings on hemodynamics were observed by Anis et al in their study on the laparoscopic gynecological study.[81] Xu et al, also concluded that 0.4 mcg/kg/hr infusion of dexmedetomidine caused a significant decrease in heart rate than 1.5 mg/kg/hr infusion of lignocaine, in patients undergoing laparoscopic hysterectomy.[80] However, Abd El Megid et al

observed no bradycardia or hypotension in their study despite using the same dose and duration as our study, possibly because of differences in ethnicity of their study population.[51]

Rekatsina et al, in their study, observed that 0.6 mcg/kg/hr infusion of dexmedetomidine caused a significantly lower incidence of postoperative nausea than lignocaine infusion at a dose of 1.5 mg/kg/hr.[77] However we did not observe any significant nausea in lignocaine group, possibly because of the lower dose of lignocaine or smaller sample size in our study.

Thus, the findings of our studies suggest that both infusions of dexmedetomidine and lignocaine are equi- efficacious in the management of postoperative pain following laparoscopic hysterectomy, as evidenced by similar rescue analgesic consumption in the postoperative period.

However, patients on dexmedetomdine infusion were more sedated (higher Ramsay sedation score) and had greater incidence of adverse effects like bradycardia and hypotension.

LIMITATIONS:-

- The main consideration of perioperative lignocaine use is to achieve therapeutic effects without reaching toxic serum level (> 5 mcg/ml) . One of the major limitation of our study was that serum level of lignocaine was not measured but the dose of lignocaine for bolus and subsequent infusion used in current study was used safely in multiple previous studies.
- Effect of these drugs was not studied in hypertensive and cardiac patients as these patients were excluded from study although they have a priority of pain control.
- Furthermore, ours was not a dose finding study.
- Since many patients complained of shoulder pain as well as abdominal pain after laparoscopic hysterectomy, it would have been better if

shoulder pain and postoperative pain on movement were also observed during the study. Further studies can be designed to evaluate the above mentioned aspects.

Thus we conclude , on the basis of our study that both lignocaine and dexmedetomidine provide similar pain relief, however dexmedetomidine has more adverse effects so a more vigilant and rigorous monitoring is required in this group of patients.

SUMMARY AND CONCLUSION

The present study was conducted in the Department of Anaesthesiology, Dayanand Medical College and Hospital, Ludhiana after approval from Institutional Ethics Committee. Sixty ASA I and II patients, between 35 to 60 years of age, posted for total laparoscopic hysterectomy under general anaesthesia were enrolled for this prospective, double blinded, randomized controlled trial. The patients were randomly divided into two groups of 30 patients each. The anaesthetic technique was standardized in both the study groups. Patients were administered the study drugs intravenously, each diluted to make a volume of 20 ml, given over 10 min as a loading dose in pre-induction period, and then diluted to make a volume of 50 ml, given as maintenance dose during the entire surgical procedure and the first 24 hours after surgery.

Group A- patients were treated with lignocaine 1.5 mg/kg loading dose followed by 1mg/kg/hr maintenance dose.

Group B- Patients were treated with dexdexmedetomidine 1 mcg/kg/hr loading dose followed by 0.6 mcg/kg/hr maintainence dose.

Measurements including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate (RR), oxygen saturation (SpO_2) and visual analogue scale (VAS) pain score were made at the following time intervals: immediately in the postoperative period and at 1,2,3,4,5,6,8,10,12,16, 20 and 24 hours. Total tramadol consumption in 24 hrs ,time of administration of first and subsequent rescue analgesic and number of times rescue analgesic needed to be given, incidence of adverse effects, number of bolus and dose given for treatment of adverse effects were also recorded.

The following observations were drawn during the study period:

- The patients in both the groups were comparable with respect to age, weight, height and ASA physical status.

- The mean HR values in the postoperative study period were comparable in both the groups till 3 hours. However, from 4th hour onwards till 24 hours, mean HR was significantly lower in the group B in comparison to group A.
- The mean SBP values in the postoperative period were similar in both the groups till 1 hour, thereafter from 2nd hour onwards till 24 hours, the mean SBP was significantly lower in group B as compared to group A. The mean DBP values in the postoperative period were similar in both the groups till first 8 hours, thereafter from 10th hour onwards till 24 hours, the mean DBP values were significantly lower in group B in comparison to group A.
- The mean oxygen saturation in both the groups was comparable, and none of the patients had any fall in oxygen saturation that might have necessitated oxygen administration.
- The mean respiratory rate was normal in all patients in both the groups at all time intervals. None of the patients required any respiratory assistance in the postoperative period.
- The mean baseline VAS scores were comparable in both the groups. In the postoperative period, at all time measurement intervals, the mean VAS scores in both the groups were similar.
- The mean opioid (tramadol) consumption in 24 hours was comparable in both the groups.
- The time to administration of first rescue analgesia was significantly longer in group B than group A.
- The time to administration of second rescue analgesia was significantly longer in group B than group A.
- The mean Ramsay sedation score in group B was significantly higher than group A in first postoperative 8 hours, thereafter from 10 hours onwards it was comparable at all time intervals till postoperative 24 hours.

- The incidence of bradycardia and hypotension was significantly higher in group B in comparison to group A. Mean atropine and mean ephedrine administered was also higher in group B than group A.

Hence, we conclude that both lignocaine and dexmedetomidine are equi-efficacious in reducing postoperative pain after total laparoscopic hysterectomy. However, use of lignocaine is advantageous as it offers a better safety profile in terms of reduced adverse effects like bradycardia, hypotension and sedation in comparison to dexmedetomidine, wherein more rigorous and vigilant monitoring would be necessitated.

BIBLIOGRAPHY

1. Ghosh D, Wipplinger P, Byrne DL. Can total laparoscopic hysterectomy replace total abdominal hysterectomy? A 5-year prospective cohort study of a single surgeon's experience in an unselected population. Gynecological Surgery. 2013;10(2):109-15.
2. Sutasanasuang S. Laparoscopic hysterectomy versus total abdominal hysterectomy: a retrospective comparative study. Journal of the Medical Association of Thailand. 2011;94(1):8.
3. Ekstein P, Szold A, Sagie B, Werbin N, Klausner JM, Weinbroum AA. Laparoscopic surgery may be associated with severe pain and high analgesia requirements in the immediate postoperative period. Annals of surgery. 2006 ;243(1):41.
4. Calderon M, Castorena G, Pasic E. Postoperative pain management after hysterectomy–a simple approach. Hysterectomy. 2012;269-81.
5. Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. Pain. 2020;161(9):1976-82.
6. Taş B, Donatsky AM, Gögenur I. Techniques to reduce shoulder pain after laparoscopic surgery for benign gynecological disease: A systematic review. Gynecological Surgery. 2013;10(3):169–75.
7. Choi JB, Kang K, Song MK, Seok S, Kim YH, Kim JE. Pain characteristics after total laparoscopic hysterectomy. International Journal of Medical Sciences. 2016;13(8):562–8.
8. Golzari SEJ, Nader ND, Mahmoodpoor A. Underlying Mechanisms of Postoperative Pain After Laparoscopic Surgery. JAMA Surg. 2016;151(3):295–296.
9. Boezaart AP, Smith CR, Chembrovich S, Zasimovich Y, Server A, Morgan G, et al. Visceral versus somatic pain: An educational

review of Anatomy and Clinical Implications. Regional Anesthesia & Pain Medicine. 2021;46(7):629–36.
10. Gibbison B, Kinsella SM. Postoperative analgesia for gynecological laparoscopy. Saudi J Anaesth. 2009;3(2):70-76.
11. Jackson SA, Laurence AS, Hill JC. Does post-laparoscopy pain relate to residual carbon dioxide? Anaesthesia. 1996;51(5):485-7.
12. Korell M, Schmaus F, Strowitzki T, Schneeweiss S, Hepp H. Surgical Laparoscopy, Endoscopy & Percutaneous Techniques. 1996;6(5):375–9.
13. Gan TJ. Poorly controlled postoperative pain: Prevalence, consequences, and prevention. Journal of Pain Research. 2017;10:2287–98.
14. Moore ND. In search of an ideal analgesic for common acute pain. Acute Pain. 2009;11(3-4):129–37.
15. Bisgaard T, Klarskov B, Kristiansen VB, Callesen T, Schulze S, Kehlet H, et al. Multi-regional local anesthetic infiltration during laparoscopic cholecystectomy in patients receiving prophylactic multi-modal analgesia: A randomized, double-blinded, placebo-controlled study. Anesthesia & Analgesia. 1999;89(4):1017-24.
16. Kehlet H, Dahl JB. The value of “multimodal” or “balanced analgesia” in postoperative pain treatment. Anesthesia & Analgesia. 1993;77(5):1048-56.
17. Kettner SC, Willschke H, Marhofer P. Does regional anaesthesia really improve outcome? British Journal of Anaesthesia. 2011;107:90–5.
18. Lauder GR. A review of intravenous lidocaine infusion therapy for paediatric acute and chronic pain management. Pain Relief–from Analgesics to Alternative Therapies. London (United Kingdom): INTECH. 2017:63-109.

19. Tang C, Xia Z. Dexmedetomidine in perioperative acute pain management: a non-opioid adjuvant analgesic. J Pain Res. 2017;11(10):1899-1904.
20. Sutton C. Past, present, and future of hysterectomy. Journal of minimally invasive gynecology. 2010;17(4):421-35.
21. Whiteman MK, Hillis SD, Jamieson DJ, Morrow B, Podgornik MN, Brett KM, ET AL. Inpatient hysterectomy surveillance in the United States, 2000-2004. American journal of obstetrics and gynecology. 2008;198(1):34-e1.
22. Agarwal P, Bindal N, Yadav R. Risks and benefits of total laparoscopic hysterectomy and the effect of learning curve on them. The Journal of Obstetrics and Gynecology of India. 2016;66(5):379-84.
23. Pitsillides C, Lashen H. Bowel Dysfunction after Hysterectomy for Benign Conditions: Meta-Analysis and Systematic Review. Fertility-oriented Female Reproductive Surgery. 2017.
24. Pinjala R, Lankala RR, Pulipati VN. Deep vein thrombosis following laparoscopic hysterectomy in a nulliparous woman. The Journal of Obstetrics and Gynecology of India. 2011;61(4):445-6.
25. Ekstein P, Szold A, Sagie B, Werbin N, Klausner JM, Weinbroum AA. Laparoscopic surgery may be associated with severe pain and high analgesia requirements in the immediate postoperative period. Ann Surg. 2006;243(1):41-6.
26. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. Anesthesia & Analgesia. 2003;97(2):534-40.
27. Katz J, Melzack R. Measurement of pain. Surg Clin North Am. 1999;79: 231-52

28. Clarke PRF, Spear PG. Reliability and sensitivity in the self assessment of well being. Bulletin of the British Psychological Society. 1964;17:18 A.
29. Caraceni A, Cherny N, Fainsinger R, Kaasa S, Poulain P, Radbruch L, ET AL. Pain measurement tools and methods in clinical research in palliative care: recommendations of an Expert Working Group of the European Association of Palliative Care. Journal of pain and symptom management. 2002;23(3):239-55.
30. Delgado DA, Lambert BS, Boutris N, McCulloch PC, Robbins AB, Moreno MR, Harris JD. Validation of digital visual analog scale pain scoring with a traditional paper-based visual analog scale in adults. Journal of the American Academy of Orthopaedic Surgeons. Global research & reviews. 2018;2(3):e088.
31. Ramsay MA. Acute postoperative pain management. Proc (BaylUniv Med Cent). 2000;13(3):244-7.
32. Lucas GNC, Leitão ACC, Alencar RL, Xavier RMF, Daher EF, Silva Junior GBD. Pathophysiological aspects of nephropathy caused by non-steroidal anti-inflammatory drugs. *J Bras Nefrol*. 2019;41(1):124-130.
33. Lirk P, Thiry J, Bonnet MP, Joshi GP, Bonnet F. Pain management after laparoscopic hysterectomy: systematic review of literature and PROSPECT recommendations. Regional Anesthesia& Pain Medicine. 2019;44(4):425-36.
34. Blanton E, Lamvu G, Patanwala I, Barron KI, Witzeman K, Tu FF, et al. Non-opioid pain management in benign minimally invasive hysterectomy: a systematic review. American Journal of Obstetrics and Gynecology. 2017;216(6):557-67.
35. Tulandi T, Krishnamurthy S, Mansour F, Suarthana E, Al-Malki G, Ballesteros LE, et al. A triple-blind randomized trial of preemptive use of gabapentin before laparoscopic hysterectomy for benign

gynaecologic conditions. Journal of Obstetrics and Gynaecology Canada. 2019;41(9):1282-8.

36. Hoskote H, Jenkins S. The Role of Intravenous Ketamine for Enhanced Recovery after Surgery (ERAS) Protocol for Acute Postoperative Pain Management after Laparoscopic Hysterectomy.
37. Takmaz O, Bastu E, Ozbasli E, Gundogan S, Karabuk E, Kocyigit M, Dede S, et al. Perioperative duloxetine for pain management after laparoscopic hysterectomy: a randomized placebo-controlled trial. Journal of Minimally Invasive Gynecology. 2020;27(3):665-72.
38. Gibbison B, Kinsella SM. Postoperative analgesia for gynecological laparoscopy. Saudi journal of anaesthesia. 2009;3(2):70.
39. Luo J, Min S. Postoperative pain management in the post anesthesia care unit: an update. Journal of pain research. 2017;10:2687.
40. Vadivelu N, Kai AM, Dai F, Dabu-Bondoc S. Analysis of Multiple Routes of Analgesic Administration in the Immediate Postoperative Period: A 10-Year Experience. Current Pain and Headache Reports. 2019;23(3):1-8.
41. Puntillo F, Giglio M, Varrassi G. The Routes of Administration for Acute Postoperative Pain Medication. Pain and Therapy. 2021;10(2):909-25.
42. Kaur M, Singh PM. Current role of dexmedetomidine in clinical anesthesia and intensive care. *Anesth Essays Res*. 2011;5(2):128-133.
43. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: a novel sedative-analgesic agent. *Proc (BaylUniv Med Cent)*. 2001;14(1):13-21.
44. Paranjpe JS. Dexmedetomidine: Expanding role in anesthesia. Med J DY Patil Univ. 2013;6:5-13
45. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs. 2000;59(2):263-8.

46. Naaz S, Ozair E. Dexmedetomidine in current anaesthesia practice-a review. Journal of clinical and diagnostic research: JCDR. 2014;8(10):1.
47. Ge DJ, Qi B, Tang G, Li JY. Intraoperative dexmedetomidine promotes postoperative analgesia and recovery in patients after abdominal hysterectomy: a double-blind, randomized clinical trial. Scientific reports. 2016;6(1):1-7.
48. Aho MS, Erkola OA, Scheinin H, Lehtinen AM, Korttila KT. Effect of intravenously administered dexmedetomidine on pain after laparoscopic tubal ligation. Anesthesia and analgesia. 1991;73(2):112-8.
49. Naik BI, Nemergut EC, Kazemi A, Fernández L, Cederholm SK, McMurry TL, et al. The effect of dexmedetomidine on postoperative opioid consumption and pain after major spine surgery. Anesthesia & Analgesia. 2016;122(5):1646-53
50. Sarkar A, Tripathi RK, Choubey S, Singh RB, Awasthi S. Comparison of effects of intravenous clonidine and dexmedetomidine for blunting pressor response during laryngoscopy and tracheal intubation: A randomized control study. Anesthesia, Essays and Researches. 2014;8(3):361-6.
51. Abd El Megid, Nassar AM. The analgesic and sedative properties of dexmedetomidine infusion after uvulopalatopharyngoplasty. The Egyptian Journal of Hospital Medicine. 2009;36(1):421-33.
52. Priye S, Jagannath S, Singh D, Shivaprakash S, Reddy DP. Dexmedetomidine as an adjunct in postoperative analgesia following cardiac surgery: a randomized, double-blind study. Saudi Journal of Anaesthesia. 2015;9(4):353.
53. Dhawan S, Aeron N, Bhambhu B. Comparison of Two Different Low Doses of Intravenous Dexmedetomidine Infusion in Patients for Abdominal Hysterectomy under Combined Spinal-Epidural

Anaesthesia. Journal of Medical Science and Clinical Research. 2020;8(6):42-7.

54. Ye Q, Wang F, Xu H, Wu L, Gao X. Effects of dexmedetomidine on intraoperative hemodynamics, recovery profile and postoperative pain in patients undergoing laparoscopic cholecystectomy: a randomized controlled trial. BMC anesthesiology. 2021;21(1):1-10.
55. Rabie A, Abdelfattah MR. Outcome of intraoperative dexmedetomidine infusion in laparoscopic cholecystectomy. Egyptian Journal of Anaesthesia. 2022;38(1):16-22.
56. Dailey RW, Leatherman JW, Sprenkle MD. Dexmedetomidine in the management of alcohol withdrawal and alcohol withdrawal delirium. InB49. Intensive Care Unit Management. 2011:A3164.
57. Castillo RL, Ibacache M, Cortínez I, Carrasco-Pozo C, Farías JG, Carrasco RA, et al. Dexmedetomidine improves cardiovascular and ventilatory outcomes in critically ill patients: basic and clinical approaches. Frontiers in Pharmacology. 2020:1641.
58. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. The Journal of the American Society of Anesthesiologists. 2000;93(2):382-94.
59. Weinberg L, Peake B, Tan C, Nikfarjam M. Pharmacokinetics and pharmacodynamics of lignocaine: A review. World J Anesthesiol. 2015;4(2):17-29
60. Foo I, Macfarlane AJR, Srivastava D, Bhaskar A, Barker H, Knaggs R, et al. The use of intravenous lidocaine for postoperative pain and recovery: international consensus statement on efficacy and safety. Anaesthesia. 2021;76(2):238-250
61. Tetzlaff JE. The pharmacology of local anesthetics. AnesthesiolClin North Am. 2000;18(2):217-33
62. Benowitz NL, Meister W. Clinical pharmacokinetics of lignocaine. Clin Pharmacokinet. 1978;3(3):177-201.

63. Bill TJ, Clayman MA, Morgan RF, Gampper TJ. Lidocaine metabolism pathophysiology, drug interactions, and surgical implications. Aesthetic Surgery Journal. 2004;24(4):307-11.
64. Eipe N, Gupta S, Penning JJ. Intravenous lidocaine for acute pain: an evidence-based clinical update. Bja Education. 2016;16:292-8.
65. Szmuk P, Farrow-Gillespie A, Sheeran P, Ezri T. The sedative effect of high dose lidocaine. Anesthesia & Analgesia. 2007;104(6):1613.
66. Krishna Murthy TK, PV VK. Effect of Perioperative Intravenous Lignocaine Infusion on Haemodynamic Responses and postoperative Analgesia in Laparoscopic Cholecystectomy Surgeries. Anesthesiology and Pain Medicine. 2018;8(2):e63490.
67. Dewinter G, Moens P, Fieuws S, Vanaudenaerde B, Van de Velde M, Rex S. Systemic lidocaine fails to improve postoperative morphine consumption, postoperative recovery and quality of life in patients undergoing posterior spinal arthrodesis. A double-blind, randomized, placebo-controlled trial. BJA: British Journal of Anaesthesia. 2017;118(4):576-85.
68. Ho ML, Kerr SJ, Stevens J. Intravenous lidocaine infusions for 48 hours in open colorectal surgery: a prospective, randomized, double-blinded, placebo-controlled trial. Korean Journal of Anesthesiology. 2018;71(1):57.
69. Sarakatsianou C, Perivoliotis K, Tzovaras G, Samara AA, Baloyiannis I. Efficacy of Intravenous Use of Lidocaine in Postoperative Pain Management After Laparoscopic Colorectal Surgery: A Meta-analysis and Meta-regression of RCTs. in vivo. 2021;35(6):3413-21.
70. Tauzin-Fin P, Bernard O, Sesay M, Biais M, Richebe P, Quinart A, Revel P, Sztark F. Benefits of intravenous lidocaine on post-operative pain and acute rehabilitation after laparoscopic

nephrectomy. Journal of anaesthesiology, clinical pharmacology. 2014;30(3):366-72.

71. Lahiri S, Das S, Basu SR. Intraoperative lignocaine infusion achieving earlier discharge criteria among laparoscopic cholecystectomy patients. Saudi J Laparosc. 2018;3:16-20.
72. : Augustine A, Philip S. Effect of perioperative intravenous lignocaine infusion on postoperative pain in laparoscopic cholecystectomy. J AnesthCrit Care Open Access. 2021;13(1):22–28.
73. Ibrahim A, Aly M, Farrag W. Effect of intravenous lidocaine infusion on long-term postoperative pain after spinal fusion surgery. Medicine. 2018;97(13):e0229.
74. Lee U, Choi YJ, Choi GJ, Kang H. Intravenous lidocaine for effective pain relief after bimaxillary surgery. Clinical Oral Investigations. 2017;21(9):2645-52.
75. Kim KT, Cho DC, Sung JK, Kim YB, Kang H, Song KS, et al. Intraoperative systemic infusion of lidocaine reduces postoperative pain after lumbar surgery: a double-blinded, randomized, placebo-controlled clinical trial. The Spine Journal. 2014;14(8):1559-66.
76. Page N. Intravenous lignocaine infusion for intractable pain in Ewing's sarcoma. Indian Journal of Palliative Care. 2018;24(1):115.
77. Rekatsina M, Theodosopoulou P, Staikou C. Effects of Intravenous Dexmedetomidine Versus Lidocaine on Postoperative Pain, Analgesic Consumption and Functional Recovery After Abdominal Gynecological Surgery: A Randomized Placebo-controlled Double Blind Study. Pain Physician. 2021;24(7):E997-1006.
78. Menshawi MA, Fahim HM. Dexmedetomidine versus lidocaine as an adjuvant to general anesthesia for elective abdominal gynecological surgeries. Ain-Shams Journal of Anesthesiology. 2019;11(1):1-9.

79. Cho K, Lee W, Lee JH, Kim MH, Lee KM. Perioperative infusion of lidocaine vs. dexmedetomidine; effect on reduction of postoperative analgesics consumption after laparoscopic cholecystectomy: 14AP5-7. European Journal of Anaesthesiology| EJA. 2014;31:228.
80. Xu SQ, Li YH, Wang SB, Hu SH, Ju X, Xiao JB. Effects of intravenous lidocaine, dexmedetomidine and their combination on postoperative pain and bowel function recovery after abdominal hysterectomy. Minerva anestesiologica. 2017;83(7):685-94.
81. Anis SG, Samir GM, ElSerwi HB. Lidocaine versus dexmedetomidine infusion in diagnostic laparoscopic gynecologic surgery: a comparative study. Ain-Shams Journal of Anaesthesiology. 2016;9(4):508.
82. 82) Kumari A, Acharya B, Ghimire B, Shrestha A. Post-operative analgesic effect of intraperitoneal ropivacaine with or without tramadol in laparoscopic cholecystectomy. Indian Journal of Anaesthesia. 2020;64(1):43.
83. Mohammed NS, Habib MK, Abbas EA, Mahmoud SM, Ramadan IA. Comparative study between the effect of dexmedetomidine and lidocaine infusion in lumbar fixation on hemodynamics, fentanyl requirements, and postoperative analgesia. Ain-Shams Journal of Anesthesiology. 2020;12(1):1-9.
84. Andjelković L, Novak-Jankovič V, Požar-Lukanovič N, Bosnić Z, Spindler-Vesel A. Influence of dexmedetomidine and lidocaine on perioperative opioid consumption in laparoscopic intestine resection: a randomized controlled clinical trial. Journal of International Medical Research. 2018;46(12):5143-54..
85. Shivaji P, Agrawal S, Kumar A, Bahadur A. Evaluation of lignocaine, dexmedetomidine, lignocaine-dexmedetomidine infusion on pain and quality of recovery for robotic abdominal hysterectomy: a prospective randomized controlled trial. Brazilian Journal of Anesthesiology. 2021:S0104-14.

86. Olgin JE, Zipes DP. Specific arrhythmias: Diagnosis and Treatment. In: Mann DL, Zipes DP, Libby P, Bonow RP, Braunwald E. Braunwald's Heart Disease. Philadelphia: Elsevier- Saunders; 2015. p. 748-52.
87. KlÖHR S, Roth R, Hofmann T, Rossaint R, Heesen M. Definitions of hypotension after spinal anaesthesia for caesarean section: literature search and application to parturients. Acta Anaesthesiologica Scandinavica. 2010;54(8):909-21.
88. Sessler CN, Grap MJ, Ramsay MA. Evaluating and monitoring analgesia and sedation in the intensive care unit. Critical care. 2008;12(3):1-3.
89. Abdallah FW, Abrishami A, Brull R. The facilitatory effects of intravenous dexmedetomidine on the duration of spinal anesthesia: a systematic review and meta-analysis. Anesthesia & Analgesia. 2013;117(1):271-8.

Sr.no	Group	MRD No.	Age (years)	ASA grade	Height (cm)	Weight (kg)	BMI	Gender	Date of admssion	Anaesthesia start time	Surgery start	Surgery finish	Anaesthesia finish	Duration (hour)	Baseline HR(bpm)	Baseline RR (per min)	Baseline SpO2(%)	Baseline SBP (mmHg)	Baseline DBP (mmHg)	Baseline MAP (mmHg)	Systolic immediate postoperative period	Systolic 1 hour (mmHg)	Systolic 2 hours (mmHg)	Systolic 3 hours (mmHg)	Systolic 4 hours (mmHg)	Systolic 5 hours (mmHg)	Systolic 6 hours (mmHg)	Systolic 8 hours (mmHg)	Systolic 10 hours (mmHg)	Systolic 12 hours (mmHg)	Systolic 16 hours (mmHg)
1	B	876821	49	II	162.56	82	31	F	6/1/2020	9:30am	9:45am	11:40am	12pm	2:30	92	16	100	127	78	97	136	132	127	122	120	125	130	126	124	120	116
2	A	860607	49	II	157.48	73	29	F	10/1/2020	1:30pm	1:45pm	3:30pm	4pm	2:30	96	16	99	132	82	102	140	142	138	138	137	125	117	137	135	137	131
3	B	880580	42	II	165	64	23.5	F	14/1/2020	9:45am	10:00 AM	12:10pm	12:30 PM	2:45	90	16	98	135	74	99	144	142	136	132	130	128	126	124	120	122	120
4	B	793632	43	II	157.48	60	24.2	F	16/1/2020	10:00 AM	10:15AM	1:00pm	1:15 PM	3:15	86	16	99	124	72	92	142	130	122	116	108	102	96	126	124	120	116
5	A	713742	45	II	162.56	66	25	F	28/1/2020	11:15am	11:30am	1:45pm	2:00pm	2:45	90	16	98	129	75	97	138	142	134	132	131	131	127	129	131	127	125
6	B	890535	37	I	160	62	24.2	F	29/1/2020	9:40 AM	10:00 AM	12:30 PM	12:40pm	3:00	90	16	100	126	87	101	136	134	132	130	126	122	118	116	114	116	112
7	A	738309	42	I	152.4	58	25	F	1/2/2020	9:45 AM	10:00 AM	12:40 PM	1:00pm	3:15	88	16	99	112	58	80	128	130	128	126	119	119	115	113	111	111	109
8	B	208207	39	II	157.48	60	24.2	F	4/2/2020	11:15 AM	11:35 AM	1:30 PM	1:45 PM	2:30	86	16	98	112	58	80	120	118	116	116	114	112	110	96	92	86	120
9	A	682978	39	II	160	64	25	F	6/2/2020	11:45 AM	12:00 PM	2:35pm	3:00pm	3:15	86	18	99	118	69	89	126	128	126	126	119	119	119	117	117	115	115
10	A	909713	51	II	162.56	68	25.7	F	7/2/2020	12:15 PM	12:30 PM	3:00pm	3:15 PM	3:00	68	18	98	132	68	84	146	146	144	144	137	135	135	133	133	131	131
11	A	910254	45	I	157.48	60	24.2	F	8/2/2020	11:15AM	11:30 AM	1:30PM	1:45PM	2:30	78	18	100	136	77	104	150	148	148	146	142	139	137	137	135	135	133
12	A	909775	46	II	162.56	68	25.7	F	10/2/2020	12:30PM	12:50PM	2:30PM	2:45PM	2:15	76	18	99	127	64	86	140	138	138	136	129	125	123	127	125	125	124
13	A	938456	46	II	160	62	24.2	F	11/2/2020	9:10AM	9:35AM	11:40AM	12PM	2:50	76	18	98	133	82	103	145	142	142	140	135	133	133	131	131	129	129
14	A	941464	45	I	162.56	66	25.7	F	13/2/2020	9:30AM	9:50AM	11:50AM	12PM	2:30	88	18	98	118	78	96	130	128	126	124	121	117	121	123	119	115	113
15	B	856399	41	I	160	62	24.2	F	21/2/2020	9:35AM	9:55AM	12:00PM	12:20PM	2:45	70	18	99	124	74	94	134	130	126	124	122	120	118	116	120	118	116
16	B	944373	48	I	157.48	60	24.2	F	23/1/2020	12:45PM	1:00PM	3:00PM	3:20PM	2:35	62	16	100	130	92	104	138	136	132	134	128	126	128	124	122	120	118
17	B	941729	42	I	157.48	66	26.6	F	27/2/2020	9:30AM	9:50AM	11:30AM	12:18 PM	2:48	76	16	98	114	52	74	122	120	117	115	113	110	96	94	88	132	128
18	B	945451	40	II	162.56	80	30.3	F	3/3/2020	1:00PM	1:20PM	3:30 PM	3:58 PM	2:58	96	16	98	136	78	103	144	140	138	136	133	130	127	125	122	120	118
19	B	945664	35	II	157.48	74	29.8	F	4/3/2020	12:45PM	1:00PM	2:30PM	3:00 PM	2:15	78	16	99	132	76	100	128	122	120	118	116	114	116	114	120	110	109
20	A	545185	50	II	165	74	27.1	F	5/3/2020	12:15PM	12:30PM	2:15pm	2:30 PM	2:15	80	16	99	126	64	92	140	136	132	134	130	129	123	127	129	123	119
21	B	789672	38	II	157.48	66	26.6	F	20/3/2020	12:30PM	12:45PM	2:30PM	3:00PM	2:30	90	16	98	136	74	95	142	138	134	130	124	120	114	108	124	120	118
22	B	938456	46	I	162.56	68	25.7	F	30/6/2020	11:20AM	11:40AM	1:10 PM	1:35 PM	2:15	78	16	98	138	72	97	144	140	137	135	132	129	125	121	120	117	114
23	A	944446	40	I	165	60	23.4	F	9/7/2020	11:40AM	12:00PM	2:10 PM	2:30 PM	2:50	82	18	99	124	70	93	142	140	142	140	139	134	133	131	133	129	125
24	B	977050	55	I	165	66	25	F	10/7/2020	11:30AM	11:50AM	1:45 PM	2:15 PM	2:45	86	18	97	116	60	88	126	121	118	115	110	106	104	100	95	99	88
25	A	676651	38	I	154.94	60	25	F	10/7/2020	9:40AM	10AM	11:35AM	12:00PM	2:20	82	14	97	124	70	93	130	130	128	126	123	121	119	121	119	119	117
26	A	982205	39	II	162.56	68	25.7	F	18/7/2020	9:30AM	9:50AM	11:30AM	11:55AM	2:25	70	18	98	124	78	98	134	132	134	132	129	127	129	130	129	127	129
27	B	987578	37	I	160	62	24.2	F	21/7/2020	11:35AM	11:55AM	1:30AM	1:50PM	2:15	94	18	98	136	66	95	142	139	136	132	129	125	120	114	105	126	122
28	B	545185	50	I	162.56	66	25.7	F	31/7/2020	9:30AM	9:50AM	11:50AM	12PM	2:30	94	18	99	134	82	104	143	140	137	134	130	129	126	124	128	132	135
29	A	1005936	50	I	160	62	24.2	F	31/7/2020	9:35AM	9:55AM	12:20 PM	12:40 PM	3:05	80	18	99	120	66	92	134	134	132	130	125	123	122	123	121	121	119
30	B	950573	48	II	162.56	68	25.7	F	20/8/2020	12:15 PM	12:30 PM	3:00pm	3:15 PM	3:00	84	16	98	136	83	103	142	146	143	141	139	135	131	128	130	126	121
31	A	1006789	42	I	157.48	60	24.2	F	20/8/2020	11:15AM	11:30 AM	1:35 PM	1:50 PM	2:35	68	16	96	132	96	108	142	138	136	140	131	129	125	125	127	129	125
32	B	1008358	42	II	162.56	68	25.7	F	10/9/2020	12:30PM	12:50PM	2:35 PM	2:55 PM	2:25	92	16	97	126	89	102	134	132	129	126	121	118	116	118	114	116	114
33	B	963998	26	II	160	62	24.2	F	10/9/2020	9:10AM	9:35AM	11:40AM	12PM	2:50	92	16	98	138	88	106	146	143	140	137	134	131	128	126	123	119	123
34	A	306319	47	I	162.56	66	25.7	F	19/9/2020	9:30AM	9:50AM	11:50AM	12:09 PM	2:49	64	16	99	120	70	72	130	136	132	132	125	123	121	119	119	117	115
35	A	1029187	45	I	160	62	24.2	F	20/10/2020	9:35AM	9:55AM	12:00PM	12:30 PM	2:55	92	16	100	136	82	96	150	148	146	146	139	135	137	135	135	133	131
36	A	973153	54	I	157.48	60	24.2	F	23/10/2020	12:45PM	1:00PM	3:00PM	3:20PM	2:35	62	18	98	110	70	92	130	120	124	122	119	115	117	115	113	113	111
37	A	1031176	46	I	157.48	66	26.6	F	2/11/2020	9:30AM	9:50AM	11:30AM	11:50AM	2:20	120	14	96	132	83	102	140	138	136	134	131	129	130	127	125	125	123
38	B	1034134	50	II	162.56	80	30.3	F	18/11/2020	1:00PM	1:20PM	3:30pm	3:45 PM	2:45	76	18	97	106	75	78	114	111	108	103	100	97	94	91	90	84	124
39	A	1009199	34	II	157.48	74	29.8	F	22-12-2020	12:45PM	1:00PM	2:30PM	3:15 PM	2:30	77	14	99	128	70	90	138	136	134	134	125	127	125	123	123	121	120
40	B	1038755	52	II	165	74	27.1	F	29/12/2020	12:15PM	12:30PM	2:45 PM	3:00 PM	2:45	72	14	100	126	86	98	134	131	128	125	122	119	117	121	125	124	121
41	B	1027334	52	II	157.48	66	26.6	F	31/12/2020	12:30PM	12:45PM	2:30PM	2:55PM	2:25	78	14	98	140	82	96	148	145	140	136	132	128	125	122	118	121	118
42	B	1012421	47	I	162.56	68	25.7	F	18/1/2021	11:20AM	11:40AM	1:45PM	2:00PM	2:40	92	18	99	136	70	102	144	138	132	126	122	118	114	112	108	106	126
43	A	789925	53	I	160	60	23.4	F	6/2/2021	11:40AM	12:00PM	1:30PM	2:20PM	2:30	78	18	98	130	70	96	140	142	138	136	133	131	129	131	129	127	127
44	A	1044517	42	I	162.56	66	25	F	9/2/2021	11:28Am	11:50AM	1:30pm	1:50pm	2:22	82	16	97	132	62	93	144	142	142	140	135	133	131	129	131	127	127
45	A	1032599	54	I	154.94	60	25	F	17-2-2021	9:40AM	10AM	11:50 AM	12:30 PM	2:50	86	16	97	138	78	102	146	144	145	143	137	137	135	131	133	127	125
46	A	698761	40	II	162.56	68	25.7	F	18-2-2021	9:30AM	9:50AM	11:30AM	11:55AM	2:25	71	18	98	122	75	92	132	131	128	130	122	124	123	121	120	121	119
47	A	1057697	56	I	160	62	24.2	F	21-2-2021	11:35AM	11:55AM	1:30AM	1:50PM	2:15	95	18	98	138	91	108	146	146	144	142	135	137	135	133	131	130	131
48	B	1059341	44	I	160	66	25.7	F	25/2/2020	9:30AM	9:50AM	11:50AM	12PM	2:30	96	16	99	135	89	107	150	148	145	142	138	134	131	128	124	120	116
49	B	991070	60	I	160	62	24.2	F	29/2/2020	9:35AM	9:55AM	12:00PM	12:20PM	2:45	74	14	99	135	83	100	144	141	138	133	129	133	128	125	122	124	120
50	A	1062741	51	I	160	62	24.2	F	2/3/2021	12:35pm	1:00pm	2:30pm	3:00 PM	2:25	95	14	98	138	69	96	150	145	142	140	136	133	131	131	127	125	123
51	A	1057445	43	I	157.48	60	24.2	F	4/3/2021	12:45PM	1:00PM	3:00PM	3:20PM	2:35	78	14	98	115	76	95	130	128	129	126	119	121	118	117	115	116	119
52	A	28598	47	I	157.48	66	26.6	F	6/3/2021	9:30AM	9:50AM	11:30AM	11:50AM	2:20	76	14	98	136	80	96	138	136	134	135	131	130	129	127	125	123	123
53	B	329307	48	II	162.56	80	30.3	F	10/3/2021	1:00PM	1:20PM	3:25 PM	3:48 PM	2:48	66	16	99	115	78	91	130	128	125	121	117	114	111	106	102	96	88
54	B	1078575	45	II	157.48	74	29.8	F	16/3/2021	12:45PM	1:00PM	2:40pm	3:05 PM	2:20	128	16	99	135	75	97	144	141	138	135	131	127	123	120	123	126	130
55	A	1038005	43	II	165	74	27.1	F	20-3-2021	12:15PM	12:30PM	2:45 PM	3:00 PM	2:45	92	18	97	138	67	100	140	138	136	136	130	129	127	125	124	121	123
56	B	1059341	44	II	157.48	66	26.6	F	26/3/2021	12:30PM	12:45PM	2:30PM	3:00PM	2:30	83	18	97	132	89	108	140	137	134	130	127	125	123	119	122	117	114
57	B	1088317	46	I	162.56	68	25.7	F	30-3-2021	10:38am	11:05 AM	1:00PM	1:20PM	2:42	66	16	96	137	85	105	144	141	137	132	128	124	121	118	116	112	108
58	B	970805	50	I	160	60	23.4	F	8/4/2021	11:40AM	12:00PM	1:30PM	2:00pm	2:20	83	16	96	131	82	104	138	132	126	122	118	112	108	98	114	112	114
59	A	1157450	48	I	162.56	66	25	F	24-8-2021	11:30AM	11:50AM	2:10 PM	2:30 PM	3:00	82	18	98	136	91	107	144	143	142	140	135	133	131	131	129	131	129
60	B	823952	49	I	154.94	60	25	F	24-8-2021	9:40AM	10AM	11:35AM	12:00PM	2:20	96	18	98	130	87	98	140	138	134	130	127	123	120	116	112	115	113

Sr.no	Group	MRD No.	Systolic 20 hours (mmHg)	Systolic 24 hours (mmHg)	DIASTOLIC immediate postoperative period (mmHg)	DIASTOLIC 1 hour (mmHg)	DIASTOLIC 2 hours (mmHg)	DIASTOLIC 3 hours (mmHg)	DIASTOLIC 4 hours (mmHg)	DIASTOLIC 5 hours (mmHg)	DIASTOLIC 6 hours (mmHg)	DIASTOLIC 8 hours (mmHg)	DIASTOLIC 10 hours (mmHg)	DIASTOLIC 12 hours (mmHg)	DIASTOLIC 16 hours (mmHg)	DIASTOLIC 20 hours (mmHg)	DIASTOLIC 24 hours (mmHg)	HR immediate postoperative period (bpm)	HR 1 hour (bpm)	HR 2 hours (bpm)	HR 3 hours (bpm)	HR 4 hours (bpm)	HR 5 hours (bpm)	HR 6 hours (bpm)	HR 8 hours (bpm)	HR 10 hours (bpm)	HR 12 hours (bpm)	HR 16 hours (bpm)	HR 20 hours (bpm)	HR 24 hours (bpm)	SPO2 immediate postoperative period (%)
1	B	876821	120	118	84	82	80	76	77	70	80	77	70	68	66	70	68	100	102	95	93	92	86	83	80	76	78	72	68	64	99
2	A	860607	125	127	80	77	70	80	74	71	72	70	68	70	70	77	74	100	99	100	98	96	96	91	90	88	92	92	90	92	99
3	B	880580	118	116	82	80	78	75	75	76	78	75	68	66	64	62	60	94	96	93	90	86	85	82	80	76	72	68	62	60	98
4	B	793632	112	110	80	78	76	74	58	56	54	60	64	60	62	64	66	96	94	87	85	81	77	73	70	68	69	67	65	62	98
5	A	713742	123	119	82	78	72	80	68	66	70	69	76	76	75	74	74	99	96	94	90	92	90	88	87	86	88	86	86	85	98
6	B	890535	108	110	90	91	90	86	74	73	72	72	76	74	72	70	72	96	95	92	90	84	81	78	75	71	68	64	62	64	99
7	A	738309	109	107	68	60	58	56	68	66	66	65	58	58	60	60	58	94	92	92	91	90	89	91	82	80	85	84	83	82	99
8	B	208207	118	115	70	68	64	68	68	68	69	70	60	54	78	76	72	79	77	86	82	78	76	72	69	68	70	66	62	61	99
9	A	682978	121	115	78	76	76	75	80	78	78	78	70	70	69	69	68	96	100	94	91	90	85	84	85	84	83	83	82	81	99
10	A	909713	129	129	76	71	70	69	62	58	58	61	72	70	70	72	70	92	89	77	78	77	76	72	71	71	70	70	68	66	98
11	A	910254	133	129	84	82	80	79	66	68	72	71	76	74	76	74	74	76	72	84	84	82	82	76	72	70	68	70	68	64	97
12	A	909775	123	123	78	72	70	64	86	88	86	85	64	64	65	66	68	70	68	96	90	86	79	72	71	68	66	62	64	65	99
13	A	938456	130	131	90	88	86	88	60	58	59	59	80	82	80	82	82	82	78	84	82	82	80	76	74	74	72	72	70	66	99
14	A	941464	113	115	88	86	87	84	74	72	78	77	78	78	76	76	78	102	104	95	94	96	95	90	91	92	91	90	91	88	98
15	B	856399	114	116	82	80	76	72	78	78	78	76	70	68	64	62	60	85	85	70	68	64	60	54	86	72	70	66	64	60	98
16	B	944373	116	114	96	96	94	92	68	66	70	68	84	82	80	79	76	98	98	64	57	90	85	79	72	65	57	82	75	66	99
17	B	941729	124	118	74	72	70	68	84	84	82	80	50	76	74	70	68	84	85	74	70	68	65	64	60	54	90	85	78	70	100
18	B	945451	116	114	86	84	82	80	80	80	78	79	80	76	74	72	70	98	96	100	95	90	88	82	80	78	74	75	70	65	99
19	B	945664	126	120	84	81	78	75	70	68	70	72	72	70	72	74	72	100	98	80	76	72	68	64	60	54	86	76	72	68	97
20	A	545185	121	125	74	72	70	72	68	66	70	73	72	68	66	68	69	86	82	94	86	88	84	78	76	74	70	71	72	70	99
21	B	789672	120	112	82	80	78	76	72	68	64	60	68	66	68	70	68	100	91	88	86	84	80	76	72	78	70	68	64	60	99
22	B	938456	112	110	80	78	76	75	74	72	72	70	66	64	66	68	70	94	90	82	77	73	69	66	60	53	85	80	76	70	98
23	A	944446	123	121	76	72	76	78	72	66	70	69	74	72	72	74	72	98	98	88	84	92	90	80	82	82	81	80	79	77	98
24	B	977050	130	126	68	66	65	64	84	82	86	84	63	60	54	60	62	79	78	87	83	80	76	70	64	68	64	68	62	60	99
25	A	676651	117	115	80	76	76	74	69	67	68	67	70	72	71	72	70	87	85	89	85	88	82	79	80	80	76	79	74	76	100
26	A	982205	125	123	86	84	85	86	59	58	59	61	82	84	80	82	80	95	92	76	78	75	74	71	72	70	71	72	74	70	99
27	B	987578	120	118	74	72	71	69	70	70	68	68	56	63	65	63	62	90	88	93	90	85	81	76	72	68	62	66	60	62	98
28	B	545185	129	128	90	89	88	86	96	94	94	96	76	73	75	73	71	75	76	96	90	85	79	73	69	65	66	64	65	63	98
29	A	1005936	121	115	78	76	73	72	63	61	61	61	66	68	68	66	68	102	95	89	86	85	84	79	78	77	77	76	76	74	99
30	B	950573	119	117	88	87	85	83	76	75	74	75	71	68	70	68	65	70	78	86	83	79	75	69	72	68	65	62	60	61	98
31	A	1006789	123	123	100	98	98	96	80	78	78	78	96	94	92	92	90	103	105	70	74	70	69	64	60	62	61	60	62	65	99
32	B	1008358	115	110	96	95	93	92	85	86	85	84	80	76	74	75	72	98	98	99	93	89	84	81	78	73	69	72	66	63	98
33	B	963998	120	117	94	94	92	90	74	70	72	70	80	79	76	75	73	75	75	98	95	91	83	78	72	66	62	54	86	78	97
34	A	306319	117	115	82	80	74	74	77	74	73	72	74	74	72	70	70	95	89	75	74	72	70	66	64	62	61	61	60	64	98
35	A	1029187	129	129	90	90	88	84	86	84	84	81	80	82	80	80	82	100	104	96	96	94	92	86	82	84	78	76	76	74	99
36	A	973153	111	109	80	79	75	76	82	84	82	81	72	70	68	69	70	99	105	72	72	71	70	66	64	60	58	60	61	62	99
37	A	1031176	123	121	90	86	85	88	66	64	62	61	75	72	70	75	74	84	89	106	102	100	98	95	92	91	92	90	93	92	97
38	B	1034134	119	115	84	80	76	74	84	82	80	79	60	52	68	65	62	110	108	82	76	74	72	71	75	70	68	64	62	63	98
39	A	1009199	121	122	80	78	76	75	82	79	79	78	72	70	70	68	68	80	74	82	81	80	81	78	76	79	78	76	77	78	99
40	B	1038755	116	118	92	92	90	88	76	79	75	74	78	76	74	72	70	84	83	70	65	61	54	90	82	74	69	58	66	68	99
41	B	1027334	116	114	90	88	86	84	77	76	72	74	74	72	70	68	66	90	82	91	86	83	78	73	69	64	61	62	64	69	99
42	B	1012421	118	116	78	76	74	72	70	68	66	64	62	58	66	64	62	96	95	93	88	84	81	78	74	71	68	65	62	68	98
43	A	789925	125	127	80	78	79	78	78	76	76	75	73	72	72	70	68	87	95	83	84	82	82	76	78	77	78	76	76	74	99
44	A	1044517	125	125	78	74	72	76	66	68	66	65	70	68	66	68	65	104	98	96	95	89	88	81	80	79	76	74	71	68	98
45	A	1032599	127	129	86	85	84	83	86	84	84	83	84	82	80	82	81	104	106	84	86	85	82	76	76	74	75	73	71	72	99
46	A	698761	119	117	86	82	80	78	78	76	76	75	75	72	78	75	72	86	90	85	82	84	80	77	74	72	73	71	70	72	98
47	A	1057697	133	131	100	98	96	94	68	66	66	65	88	86	88	87	89	73	70	98	97	96	95	90	88	86	85	85	86	86	99
48	B	1059341	112	114	97	96	94	92	82	81	80	82	82	80	78	76	73	86	85	97	93	88	86	82	76	75	76	74	73	70	99
49	B	991070	122	118	90	88	86	84	76	75	76	74	74	70	72	70	68	80	86	85	81	78	74	71	68	65	61	65	62	60	97
50	A	1062741	123	121	78	75	74	70	70	67	68	67	70	69	68	70	69	114	116	98	99	98	97	92	91	90	88	87	86	88	99
51	A	1057445	117	115	86	82	80	81	86	84	84	83	76	75	74	75	76	90	96	85	82	86	84	78	76	77	76	74	71	75	99
52	A	28598	119	121	90	88	86	85	79	77	78	77	80	78	78	76	74	72	67	78	79	80	79	77	73	72	71	70	69	68	98
53	B	329307	92	96	82	78	76	74	94	90	88	91	64	60	54	64	60	102	100	67	63	60	64	60	52	79	70	65	59	84	97
54	B	1078575	128	124	84	81	78	76	72	74	70	68	65	62	60	62	64	102	100	110	95	91	87	83	82	80	77	72	76	72	98
55	A	1038005	125	127	76	74	72	70	77	76	76	75	66	64	62	60	62	102	105	96	98	96	94	88	88	86	84	82	83	84	98
56	B	1059341	118	120	97	96	94	92	82	80	78	79	80	85	82	80	82	90	89	91	86	83	78	74	71	68	73	67	64	66	99
57	B	1088317	112	110	91	90	88	86	84	86	83	82	76	74	70	72	74	84	80	62	60	52	86	82	78	75	71	67	72	68	100
58	B	970805	116	112	86	82	78	74	70	66	60	54	75	73	71	68	70	100	98	99	94	90	87	82	79	76	73	69	72	73	99
59	A	1157450	131	129	98	96	97	96	80	77	77	76	96	97	97	96	97	99	103	88	87	86	87	82	81	82	81	80	81	82	98
60	B	823952	110	112	92	92	90	87	95	94	95	96	75	73	71	69	67	90	89	98	93	89	86	82	78	72	67	69	73	76	99

Sr.no	Group	MRD No.	SPO2 1 hour (%)	SPO2 2 hours (%)	SPO2 3 hours (%)	SPO2 4 hours (%)	SPO2 5 hours (%)	SPO2 6 hours (%)	SPO2 8 hours (%)	SPO2 10 hours (%)	SPO2 12 hours (%)	SPO2 16 hours (%)	SPO2 20 hours (%)	SPO2 24 hours (%)	RR immediate postoperative period	RR 1 hour	RR 2 hours	RR 3 hours	RR 4 hours	RR 5 hours	RR 6 hours	RR 8 hours	RR 10 hours	RR 12 hours	RR 16 hours	RR 20 hours	RR 24 hours	VAS immediate postoperative period	VAS 1 hour	VAS 2 hours	VAS 3 hours	VAS 4 hours	VAS 5 hours	VAS 6 hours	VAS 8 hours	VAS 10 hours	VAS 12 hours	VAS 16 hours
1	B	876821	98	98	98	98	97	97	97	97	98	98	98	99	16	16	16	16	14	14	14	14	16	16	16	16	14	1	6	3	4	3	3	3	3	2	3	3
2	A	860607	98	97	97	98	99	99	99	98	98	99	98	99	16	18	14	15	14	15	16	17	18	16	17	18	16	1	6	3	3	5	3	3	3	2	3	3
3	B	880580	98	98	98	99	99	99	99	98	98	98	98	98	14	14	16	17	15	16	14	17	18	14	15	16	17	1	4	3	2	5	2	2	3	2	2	3
4	B	793632	98	98	98	97	97	97	97	97	97	98	98	98	16	16	16	14	14	14	14	16	16	16	16	14	14	1	5	3	3	3	5	3	3	3	3	3
5	A	713742	98	99	99	98	98	97	97	97	98	99	99	99	14	14	14	14	14	14	14	14	14	14	14	14	14	1	6	3	3	5	3	3	4	3	4	3
6	B	890535	98	98	98	98	98	98	98	98	97	97	97	97	16	16	14	14	16	16	14	16	15	15	15	15	15	1	6	3	3	5	3	2	4	4	2	3
7	A	738309	97	97	97	97	98	98	98	98	98	98	98	97	16	18	14	15	14	15	16	17	18	16	17	18	16	1	6	3	4	3	3	3	3	3	3	3
8	B	208207	99	99	99	99	99	99	98	99	98	99	99	99	16	16	16	16	16	16	16	14	14	14	14	16	16	1	3	3	3	3	3	3	3	2	2	3
9	A	682978	99	98	98	97	97	96	96	97	98	98	99	99	14	14	14	14	14	14	14	16	16	16	16	14	14	1	5	3	3	4	3	3	3	3	2	3
10	A	909713	98	98	99	99	96	98	98	97	96	98	98	99	14	14	14	14	15	15	15	15	16	16	16	16	14	1	4	3	3	3	3	4	3	2	3	3
11	A	910254	97	96	96	98	98	99	99	100	100	99	99	100	14	14	16	17	15	16	14	17	18	14	15	16	18	0	5	3	3	4	3	3	3	3	3	3
12	A	909775	98	99	98	98	97	97	97	98	98	99	98	98	14	14	14	14	16	16	16	16	18	18	18	18	18	0	6	3	3	3	5	2	3	3	2	3
13	A	938456	100	100	100	100	100	99	99	99	99	100	99	100	16	16	16	16	18	18	18	18	14	14	14	14	14	1	3	3	3	3	2	3	2	2	3	3
14	A	941464	98	97	97	98	98	97	97	96	97	97	98	98	16	18	14	15	14	15	16	17	18	16	17	18	16	0	3	3	3	3	2	3	3	3	3	3
15	B	856399	98	98	98	98	98	99	99	99	99	99	100	100	14	14	14	14	14	14	14	14	14	14	14	14	14	1	6	3	3	4	3	3	3	3	3	3
16	B	944373	98	97	97	98	99	99	99	98	98	99	98	99	16	16	14	14	16	16	14	16	15	15	15	15	15	1	5	3	3	5	2	3	3	2	3	3
17	B	941729	100	100	100	99	98	98	99	98	98	100	98	98	16	18	14	15	14	15	16	17	18	16	17	18	16	1	6	3	3	4	2	2	3	2	2	3
18	B	945451	95	98	96	98	98	96	97	97	98	97	97	96	15	15	15	15	16	16	16	16	16	14	15	14	16	0	5	3	4	3	3	3	3	4	3	3
19	B	945664	97	97	97	97	97	97	97	97	97	97	97	97	16	18	14	15	14	15	16	17	18	16	17	18	16	1	5	2	3	5	2	3	3	2	3	3
20	A	545185	98	100	99	100	99	98	100	98	99	98	100	100	18	18	18	18	18	18	16	16	16	16	16	16	16	1	6	3	3	5	2	3	3	3	3	3
21	B	789672	99	99	99	99	99	99	99	98	98	98	98	98	16	16	16	16	16	16	16	16	16	16	16	16	16	1	6	3	3	3	3	3	3	3	2	3
22	B	938456	98	98	98	98	98	98	98	98	98	98	98	98	14	14	16	17	15	16	14	17	18	14	15	16	17	0	3	3	3	3	2	3	2	2	3	3
23	A	944446	98	98	98	98	98	99	99	99	99	99	100	100	14	14	14	14	15	15	16	16	16	16	16	16	16	0	5	3	3	4	3	3	3	3	2	3
24	B	977050	98	97	97	98	99	99	99	98	98	99	98	99	16	18	14	15	14	15	16	17	18	16	17	18	16	1	5	3	3	3	2	4	3	2	3	3
25	A	676651	100	100	100	99	98	98	99	98	98	100	98	98	14	14	14	14	16	16	16	16	14	14	14	14	16	1	6	3	3	5	2	2	3	2	3	3
26	A	982205	95	98	96	98	98	96	97	97	98	97	97	96	16	16	16	14	14	14	14	16	14	14	16	16	16	1	5	3	3	3	4	3	3	3	2	3
27	B	987578	98	98	98	98	98	98	98	99	99	99	99	99	15	15	15	15	15	16	16	16	14	14	14	14	14	1	3	3	3	3	2	3	3	3	2	3
28	B	545185	98	98	98	98	98	99	99	99	98	98	98	98	16	16	16	14	14	14	14	16	16	16	16	14	14	0	5	3	3	5	3	3	3	2	3	3
29	A	1005936	98	98	98	98	98	98	98	98	97	97	97	97	14	14	14	14	16	16	16	16	18	18	18	18	18	0	4	3	3	3	3	3	2	3	3	3
30	B	950573	98	98	98	98	98	98	97	97	97	97	97	97	16	16	16	16	18	18	18	18	14	14	14	14	14	1	4	3	3	3	4	2	3	3	3	3
31	A	1006789	99	99	99	99	99	99	98	99	98	99	99	99	16	18	14	15	14	15	16	17	18	16	17	18	16	1	5	3	3	3	4	3	3	2	3	3
32	B	1008358	98	98	98	97	97	97	97	97	97	98	98	98	14	14	14	14	14	14	14	14	14	14	14	14	14	1	6	3	3	4	3	3	3	3	3	3
33	B	963998	97	97	97	97	97	97	97	97	97	97	97	97	16	16	14	14	16	16	14	16	15	15	15	15	15	1	5	3	3	4	3	3	3	3	3	3
34	A	306319	98	99	99	98	98	99	99	97	97	98	98	97	16	18	14	15	14	15	16	17	18	16	17	18	16	1	3	3	3	3	3	3	3	3	3	3
35	A	1029187	98	98	98	99	97	97	98	98	97	97	98	98	16	16	16	14	14	14	14	16	16	16	16	16	16	1	4	3	3	4	3	3	3	3	3	3
36	A	973153	98	98	99	99	98	98	98	98	99	99	99	97	14	14	14	14	16	16	16	16	18	18	18	18	18	2	6	3	3	4	3	2	3	4	3	3
37	A	1031176	98	99	97	97	98	98	97	97	98	98	97	97	16	16	16	18	18	18	18	14	14	14	14	14	14	1	5	3	3	3	3	3	3	3	2	3
38	B	1034134	98	98	98	98	98	98	98	98	98	98	98	98	16	18	14	15	14	15	16	17	18	16	17	18	16	1	4	3	3	3	3	4	3	3	3	3
39	A	1009199	98	96	98	98	97	97	98	98	99	98	98	99	14	14	15	15	15	15	15	16	16	16	16	16	14	0	6	3	2	5	3	3	4	3	3	3
40	B	1038755	99	98	98	99	100	99	99	100	99	98	99	98	14	14	14	14	14	14	14	14	14	14	14	14	14	0	3	3	3	3	2	3	3	2	3	3
41	B	1027334	98	99	98	99	99	100	100	99	98	99	98	99	16	16	14	14	16	16	14	16	15	15	15	15	15	1	6	3	3	3	4	2	3	4	3	3
42	B	1012421	98	98	98	99	100	100	99	98	98	99	99	100	16	18	14	15	14	15	16	17	18	16	17	18	16	1	4	2	3	3	2	3	3	3	3	3
43	A	789925	98	99	98	99	98	97	97	98	98	99	98	98	14	14	14	14	16	16	16	16	18	18	18	18	18	1	3	3	3	3	3	3	3	2	2	3
44	A	1044517	98	97	97	96	96	97	97	98	98	99	99	98	16	16	16	18	18	18	18	14	14	14	14	14	14	0	5	3	3	4	3	3	3	3	2	3
45	A	1032599	98	98	98	97	97	98	98	99	99	97	97	98	16	18	14	15	14	15	16	17	18	16	17	18	16	1	6	3	4	3	3	3	4	3	3	4
46	A	698761	98	99	99	98	98	97	97	97	98	97	98	98	15	15	16	16	16	16	14	14	14	14	14	14	14	1	5	2	3	4	2	2	2	2	2	3
47	A	1057697	100	99	100	99	99	98	98	99	100	98	99	98	16	16	16	16	16	16	16	16	16	16	16	16	16	1	5	2	3	4	3	3	3	3	3	3
48	B	1059341	98	98	98	99	99	99	99	98	98	99	98	98	14	16	16	14	14	16	16	14	14	16	16	14	14	0	6	3	3	4	3	3	3	3	3	3
49	B	991070	97	97	97	98	98	98	98	99	99	99	99	97	14	14	14	16	16	16	16	18	18	18	18	18	18	1	3	3	3	3	2	2	3	2	3	3
50	A	1062741	99	98	98	99	100	99	99	100	99	98	99	98	16	16	16	18	18	18	18	14	14	14	14	14	14	1	3	3	3	3	2	3	3	3	2	3
51	A	1057445	98	99	98	99	99	100	100	99	98	99	98	99	16	18	14	15	14	15	16	17	18	16	17	18	16	1	6	3	3	4	2	3	3	3	3	3
52	A	28598	98	98	98	99	100	100	99	98	98	99	99	100	14	14	14	14	14	14	14	14	14	14	14	14	14	1	6	3	3	3	3	4	3	2	3	3
53	B	329307	97	97	97	97	97	97	97	98	98	98	98	98	16	16	14	14	16	16	14	16	15	15	15	15	15	1	6	3	3	3	3	2	3	3	3	3
54	B	1078575	98	98	96	97	97	97	97	98	98	98	98	97	16	18	14	15	14	15	16	17	18	16	17	18	16	0	3	3	3	3	3	3	3	3	3	3
55	A	1038005	99	98	98	97	98	97	97	97	96	97	96	99	16	16	16	16	16	16	14	14	14	14	16	16	16	1	3	3	2	3	3	3	3	3	3	3
56	B	1059341	99	99	98	98	99	99	100	100	100	100	100	100	14	14	14	14	14	14	16	16	16	16	14	14	16	1	6	3	3	4	3	3	3	2	3	3
57	B	1088317	100	100	100	100	100	100	100	100	100	100	100	100	14	14	14	15	15	15	15	16	16	16	16	14	16	1	6	3	3	5	2	3	4	3	3	3
58	B	970805	99	99	99	99	99	99	99	99	99	99	99	99	16	18	14	15	14	15	16	17	18	16	17	18	16	0	3	3	3	3	3	2	3	3	2	3
59	A	1157450	96	97	98	96	98	98	99	100	100	99	100	99	16	16	16	14	14	14	14	16	16	16	14	14	14	1	6	3	3	5	3	3	3	3	3	3
60	B	823952	98	99	98	98	98	98	99	97	97	97	97	99	16	16	16	16	14	14	14	14	16	16	16	14	14	1	5	3	3	4	2	3	3	3	3	3

Sr.no	Group	MRD No.	VAS 20 hours	VAS 24 hours	Vas at time of first rescue analgesic	DRUG immediate postoperative period	DRUG 1 hour	DRUG 2 hours	DRUG 3 hours	DRUG 4 hours	DRUG 5 hours	DRUG 6 hours	DRUG 8 hours	DRUG 10 hours	DRUG 12 hours	DRUG 16 hours	DRUG 20 hours	vas at 2nd resc	DRUG2 immediate postoperative period	DRUG2 1 hour	DRUG2 2 hours	DRUG2 3 hours	DRUG2 4 hours	DRUG2 5 hours	DRUG2 6 hours	DRUG2 8 hours	DRUG2 10 hours
1	B	876821	2	1	6		tramadol 50mg											4				tramadol50 mg					
2	A	860607	2	1	6		tramadol 50mg											5					tramadol50 mg					
3	B	880580	2	1	4		tramadol 50mg											5					tramadol50 mg					
4	B	793632	2	1	5		tramadol 50mg											5						tramadol 50 mg				
5	A	713742	2	1	6		tramadol 50mg											5					tramadol50 mg					
6	B	890535	2	1	6		tramadol 50mg											5					tramadol50 mg					
7	A	738309	2	1	6		tramadol 50mg											4				tramadol 50 mg						
8	B	208207	2	1																								
9	A	682978	2	1	5		tramadol 50mg											4					tramadol50 mg					
10	A	909713	2	1	4		tramadol 50mg											4							tramadol 50 mg			
11	A	910254	2	1	5		tramadol 50mg											4					tramadol50 mg					
12	A	909775	2	1	6		tramadol 50 mg											5						tramadol50 mg				
13	A	938456	2	1																								
14	A	941464	2	1																								
15	B	856399	2	1	6		tramadol 50mg											4					tramadol50 mg					
16	B	944373	2	1	5		tramadol 50mg											5					tramadol50 mg					
17	B	941729	2	1	6		tramadol 50mg											4					tramadol50 mg					
18	B	945451	2	1	5		tramadol 50mg											4				tramadol50 mg						
19	B	945664	2	1	5		tramadol 50mg											5					tramadol50 mg					
20	A	545185	2	1	6		tramadol 50mg											5					tramadol50 mg					
21	B	789672	2	1	6		tramadol 50mg																					
22	B	938456	2	1																								
23	A	944446	2	1	5		tramadol 50mg											4					tramadol50 mg					
24	B	977050	2	1	5		tramadol 50mg											4							tramadol 50 mg			
25	A	676651	2	1	6		tramadol 50mg											5					tramadol50 mg					
26	A	982205	2	1	5		tramadol 50mg											4						tramadol 50 mg				
27	B	987578	2	1																								
28	B	545185	2	1	5		tramadol 50mg											5					tramadol50 mg					
29	A	1005936	2	1	4		tramadol 50 mg																					
30	B	950573	2	1	4		tramadol 50mg											4						tramadol 50 mg				
31	A	1006789	2	1	5		tramadol 50mg											4						tramadol 50 mg				
32	B	1008358	2	1	6		tramadol 50mg											4					tramadol50 mg					
33	B	963998	2	1	5		tramadol 50mg											4					tramadol50 mg					
34	A	306319	2	1																								
35	A	1029187	2	1	4		tramadol 50mg											4				tramadol 50 mg						
36	A	973153	2	1	6		tramadol 50mg											4					tramadol50 mg					
37	A	1031176	2	1	5		tramadol 50 mg																					
38	B	1034134	2	1	4		tramadol 50 mg											4							tramadol 50 mg			
39	A	1009199	2	1	6		tramadol 50mg											5					tramadol50 mg					
40	B	1038755	2	1																								
41	B	1027334	2	1	6		tramadol 50mg											4						tramadol 50 mg				
42	B	1012421	2	1	4		tramadol 50 mg																					
43	A	789925	2	1																								
44	A	1044517	2	1	5		tramadol 50mg											4					tramadol50 mg					
45	A	1032599	2	1	6		tramadol 50mg											4				tramadol 50 mg						
46	A	698761	2	1	5		tramadol 50mg											4					tramadol50 mg					
47	A	1057697	2	1	5		tramadol 50mg											4					tramadol50 mg					
48	B	1059341	2	1	6		tramadol 50mg											4					tramadol50 mg					
49	B	991070	2	1																								
50	A	1062741	2	1																								
51	A	1057445	2	1	6		tramadol 50mg											4					tramadol50 mg					
52	A	28598	2	1	6		tramadol 50mg											4							tramadol50 mg			
53	B	329307	2	1	6		tramadol 50mg																					
54	B	1078575	2	1																								
55	A	1038005	2	1																								
56	B	1059341	2	1	6		tramadol 50mg											4					tramadol50 mg					
57	B	1088317	2	1	6		tramadol 50mg											5					tramadol50 mg					
58	B	970805	2	1																								
59	A	1157450	2	1	6		tramadol 50mg											5					tramadol50 mg					
60	B	823952	2	1	5		tramadol 50mg											4					tramadol50 mg					

Sr.no	Group	MRD No.	DRUG2 12 hours	DRUG2 16 hours	DRUG2 20 hours	DRUG2 24 hours	vas @ subsequent	DRUG SUBSEQUENT 1 hour	DRUG SUBSEQUENT 2 hours	DRUG SUBSEQUENT 3 hours	DRUG SUBSEQUENT 4 hours	DRUG SUBSEQUENT 5 hours	DRUG SUBSEQUENT 6 hours	DRUG SUBSEQUENT 8 hours	DRUG SUBSEQUENT 10 hours	DRUG SUBSEQUENT 12 hours	DRUG SUBSEQUENT 16 hours	DRUG SUBSEQUENT 20 hours	drug 24 hrs	Time of 1st dose of Rescue Analgesic Requirement (minutes)	2nd (min)
1	B	876821																		76	270
2	A	860607																		62	245
3	B	880580																		75	295
4	B	793632																		78	340
5	A	713742					4,4							tramadol 50 mg		tramadol 50 mg				73	252
6	B	890535					4,4							tramadol 50 mg	tramadol 50 mg					74	270
7	A	738309																		70	190
8	B	208207																			
9	A	682978																		65	250
10	A	909713																		68	360
11	A	910254																		69	280
12	A	909775																		66	302
13	A	938456																			
14	A	941464																			
15	B	856399																		78	263
16	B	944373																		76	273
17	B	941729																		79	284
18	B	945451					4								tramadol 50 mg					77	226
19	B	945664																		75	270
20	A	545185																		61	250
21	B	789672																		73	
22	B	938456																			
23	A	944446																		64	254
24	B	977050																		74	366
25	A	676651																		67	255
26	A	982205																		64	304
27	B	987578																			
28	B	545185																		72	278
29	A	1005936																			
30	B	950573																		72	308
31	A	1006789																		70	302
32	B	1008358																		79	256
33	B	963998																		78	270
34	A	306319																			
35	A	1029187																		73	190
36	A	973153					4								tramadol 50 mg					70	255
37	A	1031176																		69	
38	B	1034134																		73	390
39	A	1009199					4							tramadol 50 mg						72	256
40	B	1038755																			
41	B	1027334					4								tramadol 50 mg					79	320
42	B	1012421																		73	
43	A	789925																			
44	A	1044517																		70	260
45	A	1032599					4,4							tramadol 50 mg			tramadol 50 mg			68	200
46	A	698761																		66	250
47	A	1057697																		64	245
48	B	1059341																		77	287
49	B	991070																			
50	A	1062741																			
51	A	1057445																		65	245
52	A	28598																		61	370
53	B	329307																		76	
54	B	1078575																			
55	A	1038005																			
56	B	1059341																		79	291
57	B	1088317					4							tramadol 50 mg						76	297
58	B	970805																			
59	A	1157450																		67	250
60	B	823952																		75	280

Sr.no	Group	MRD No.	subsequent Times	No. of time rescue analgesic given	No. of time subsequent given	DOSE	Adverse	SEDATION immediate postoperative period	SEDATION 1 hour	SEDATION 2 hours	SEDATION 3 hours	SEDATION 4 hours	SEDATION 5 hours	SEDATION 6 hours	SEDATION 8 hours	SEDATION 10 hours	SEDATION 12 hours	SEDATION 16 hours	SEDATION 20 hours	SEDATION 24 hours	I/V ATROPINE immediate postoperative period (0.01 mg/kg)	I/V ATROPINE 1 hours (0.01 mg/kg)	I/V ATROPINE 2 hours (0.01 mg/kg)	I/V ATROPINE 3 hours (0.01 mg/kg)
1	B	876821		2	0	100		3	3	3	3	3	3	2	2	2	2	2	2	1				
2	A	860607		2	0	100		2	2	2	2	2	2	2	2	2	2	2	2	2				
3	B	880580		2	0	100		3	3	3	3	3	2	2	2	2	2	2	2	2				
4	B	793632		2	0	100	hypotension	3	3	3	3	3	3	2	2	2	2	2	2	2				
5	A	713742	8hrs, 12 hrs	2	2	200		2	2	2	2	2	2	2	2	2	2	2	2	2				
6	B	890535	8 hrs, 10 hrs	2	2	200		3	3	3	3	3	3	3	2	2	2	2	2	2				
7	A	738309		2	0	100		2	2	2	2	2	2	2	2	2	2	2	2	2				
8	B	208207		0	0	0	hypotension	3	3	3	3	2	2	2	2	2	2	2	2	2				
9	A	682978		2	0	100		2	2	2	2	2	2	2	2	2	2	2	2	2				
10	A	909713		2	0	100		2	2	2	2	2	2	2	2	2	2	2	2	2				
11	A	910254		2	0	100	nausea	2	2	2	2	2	2	2	2	2	2	2	2	2				
12	A	909775		2	0	100		2	2	2	2	2	2	2	2	2	2	2	2	2				
13	A	938456		0	0	0		2	2	2	2	2	2	2	2	2	2	2	2	2				
14	A	941464		0	0	0		2	2	2	2	2	2	2	2	2	2	2	2	2				
15	B	856399		2	0	100	bradycardia	3	3	3	3	3	3	3	2	2	2	2	2	2				
16	B	944373		2	0	100	bradycardia	3	3	3	3	3	2	2	2	2	2	2	2	2				i/v atropine
17	B	941729		2	0	100	bradycardia + hypotension	3	3	3	3	3	3	3	2	2	2	2	2	2				
18	B	945451	10 hrs	2	1	150		3	3	3	3	3	2	2	2	2	2	2	2	2				
19	B	945664		2	2	100	bradycardia	3	3	3	3	2	2	2	2	2	2	2	2	2				
20	A	545185		2	0	100		2	2	2	2	3	2	2	2	2	2	2	2	2				
21	B	789672		1	0	50	hypotension	3	3	3	3	3	3	3	3	2	2	2	2	2				
22	B	938456		0	0	0	bradycardia	3	3	3	3	3	3	3	2	2	2	2	2	2				
23	A	944446		2	0	100		2	2	2	2	2	2	2	2	2	2	2	2	2				
24	B	977050		2	0	100	hypotension	3	3	3	3	3	3	3	2	2	2	2	2	2				
25	A	676651		2	0	100		2	2	2	2	2	2	2	2	2	2	2	2	2				
26	A	982205		2	0	100		2	2	2	2	2	2	2	2	2	2	2	2	2				
27	B	987578		0	0	0	hypotension	3	3	3	3	3	3	3	3	2	2	2	2	2				
28	B	545185		2	0	100		3	3	3	3	3	3	3	2	2	2	2	2	2				
29	A	1005936		0	0	0		2	2	2	2	2	2	2	2	2	2	2	2	2				
30	B	950573		2	0	100		3	3	3	3	3	2	2	2	2	2	2	2	2				
31	A	1006789		2	0	100		2	2	2	2	2	2	2	2	2	2	2	2	2				
32	B	1008358		2	0	100		3	3	3	3	2	2	2	2	2	2	2	2	2				
33	B	963998		2	0	100	bradycardia	3	3	3	3	3	2	2	2	2	2	2	2	2				
34	A	306319		0	0	0		2	2	2	2	2	2	2	2	2	2	2	2	2				
35	A	1029187		2	0	100	nausea	2	2	2	2	2	2	2	2	2	2	2	2	2				
36	A	973153	10 hrs	2	1	150		2	2	2	2	2	2	2	2	2	2	2	2	2				
37	A	1031176		1	0	50		2	2	2	2	2	2	2	2	2	2	2	2	2				
38	B	1034134		2	0	100	hypotension	3	3	3	3	3	3	2	2	2	2	2	2	2				
39	A	1009199	8 hrs	2	1	150		2	2	2	2	2	2	2	2	2	2	2	2	2				
40	B	1038755		0	0	0	bradycardia	3	3	3	3	3	3	2	2	2	2	2	2	2				
41	B	1027334	10 hrs	2	1	150		3	3	3	3	3	2	2	2	2	2	2	2	2				
42	B	1012421		1	1	50	hypotension	3	3	3	3	3	3	2	2	2	2	2	2	2				
43	A	789925		0	0	0	nausea	2	2	2	2	2	2	2	2	2	2	2	2	2				
44	A	1044517		2	0	100		2	2	2	2	2	2	2	2	2	2	2	2	2				
45	A	1032599	8 hrs, 16 hrs	2	2	200		2	2	2	2	2	2	2	2	2	2	2	2	2				
46	A	698761		2	0	100		2	2	2	2	2	2	2	2	2	2	2	2	2				
47	A	1057697		2	0	100		2	2	2	2	2	2	2	2	2	2	2	2	2				
48	B	1059341		2	0	100		3	3	3	3	3	3	2	2	2	2	2	2	2				
49	B	991070		0	0	0		3	3	3	3	3	3	2	2	2	2	2	2	2				
50	A	1062741		0	0	0		2	2	2	2	2	2	2	2	2	2	2	2	2				
51	A	1057445		2	0	100		2	2	2	2	2	2	2	2	2	2	2	2	2				
52	A	28598		2	0	100		3	3	3	3	3	3	3	2	2	2	2	2	2				
53	B	329307		1	0	50	bradycardia + hypotension	3	3	3	3	3	3	2	2	2	2	2	2	2				
54	B	1078575		0	0	0		3	3	3	3	3	3	2	2	2	2	2	2	2				
55	A	1038005		0	0	0		2	2	2	2	2	2	2	2	2	2	2	2	2				
56	B	1059341		2	0	100		3	3	3	3	3	3	3	2	2	2	2	2	2				
57	B	1088317	8 hrs	2	1	150	bradycardia	3	3	3	3	3	3	3	3	2	2	2	2	2				
58	B	970805		0	0	0	hypotension	3	3	3	3	3	3	3	3	3	2	2	2	2				
59	A	1157450		2	0	100		3	2	2	2	2	2	2	2	2	2	2	2	2				
60	B	823952		2	0	100		3	3	3	3	3	3	3	2	2	2	2	2	2				

Sr.no	Group	MRD No.	I/V ATROPINE 4 hours (0.01 mg/kg)	I/V ATROPINE 5 hours (0.01 mg/kg)	I/V ATROPINE 6 hours (0.01 mg/kg)	I/V ATROPINE 8 hours (0.01 mg/kg)	I/V ATROPINE 10 hours (0.01 mg/kg)	I/V ATROPINE 12 hours (0.01 mg/kg)	I/V ATROPINE 16 hours (0.01 mg/kg)	I/V ATROPINE 20 hours (0.01 mg/kg)	I/V ATROPINE 24 hours (0.01 mg/kg)	I/V EPHEDRINE immediate postoperative period (6mg)	I/V EPHEDRINE 1 hour (6mg)	I/V EPHEDRINE 2 hours (6mg)	I/V EPHEDRINE 3 hours (6mg)	I/V EPHEDRINE 4 hours (6mg)	I/V EPHEDRINE 5 hours (6mg)	I/V EPHEDRINE 6 hours (6mg)	I/V EPHEDRINE 8 hours (6mg)	I/V EPHEDRINE 10 hours (6mg)	I/V EPHEDRINE 12 hours (6mg)	I/V EPHEDRINE 16 hours (6mg)	I/V EPHEDRINE 20 hours (6mg)	I/V EPHEDRINE 24 hours (6mg)
1	B	876821																							
2	A	860607																							
3	B	880580																							
4	B	793632																i/v ephedrine							
5	A	713742																							
6	B	890535																							
7	A	738309																							
8	B	208207																			i/v ephedrine				
9	A	682978																							
10	A	909713																							
11	A	910254																							
12	A	909775																							
13	A	938456																							
14	A	941464																							
15	B	856399			i/v atropine																				
16	B	944373						i/v atropine																	
17	B	941729					i/v atropine													i/v ephedrine					
18	B	945451																							
19	B	945664					i/v atropine																		
20	A	545185																							
21	B	789672																	i/v ephedrine						
22	B	938456					i/v atropine																		
23	A	944446																							
24	B	977050																					i/v ephedrine		
25	A	676651																							
26	A	982205																							
27	B	987578																		i/v ephedrine					
28	B	545185																							
29	A	1005936																							
30	B	950573																							
31	A	1006789																							
32	B	1008358																							
33	B	963998							i/v atropine																
34	A	306319																							
35	A	1029187																							
36	A	973153						i/v atropine																	
37	A	1031176																							
38	B	1034134																				i/v ephedrine			
39	A	1009199																							
40	B	1038755		i/v atropine					i/v atropine																
41	B	1027334																							
42	B	1012421																				i/v ephedrine			
43	A	789925																							
44	A	1044517																							
45	A	1032599																							
46	A	698761																							
47	A	1057697																							
48	B	1059341																							
49	B	991070																							
50	A	1062741																							
51	A	1057445																							
52	A	28598																							
53	B	329307				i/v atropine				i/v atropine													i/v ephedrine		
54	B	1078575																							
55	A	1038005																							
56	B	1059341																							
57	B	1088317	i/v atropine																						
58	B	970805																	i/v ephedrine						
59	A	1157450																							
60	B	823952																							

1430
9/2/22

Sadiq Road, Faridkot (Punjab) India

Phone No 01639-256232, 36 (Reception)

Fax No 01639-256234, 256235 (Exams.)

Email-bfuhsthesis@gmail.com

No. 07-BFUHS/Exam/ 1232 Dated 9/2/2022

The Principal
DMC, Ludhiana.

Subject: **Change of Supervisor &Co-Supervisor.**

This is in reference to your office on the above mentioned subject. In this connection, you are informed that the Worthy Vice Chancellor has very kindly accepted your recommendations as mentioned below

Sr.No	Name	Specialty	Supervisor & Co-Supervisor already appointed	Present name of new Supervisor & Co-Supervisor.
1	Vasundhara jindal	Anesthesia	Sup:- Dr. Dinesh Sood, Prof, Dept of Anaesthesia Co-Sup:- Dr. Sandeep kundra, Prof, Dept of Anesthesia Dr. Ashima Teneja, Prof & Head Obst & Gynae	Sup:- Dr. Sandeep kundra, Prof, Dept of Anesthesia Co-Sup:- Dr. Anju Grewal, Prof & Head, Dept of Anaesthesia Dr. Ashima Teneja, Prof & Head Obst & Gynae

The student may be requested to attach photocopy of this letter along with plan approval letter while submitting thesis in the university. All concerned may also be informed accordingly.

Dr. S P Singh, MS (Oph)
Controler of Examinations

Baba Farid University
of Health Sciences
Sadiq Road
Faridkot-151 203 (Pb). INDIA.
Phone : 01639-256232,256236
Tele/Fax : 01639-256235
Email - Examination@bfuhs.ac.in

No. BFUHS/2K21p TH/ 5207 Date 20/4/2021

The Principal,
DMC,Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 22.01.2021 has approved the plan of thesis of **Dr. Vasundhara Jindal,** a student of your college for **MD Anaesthesiology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Comparison of intravenous infusion of lignocaine versus dexmedetomidine for postoperative pain relief in patients undergoing total laparoscopic hysterectomy

Supervisor
Dr. Dinesh Sood
Prof.,
Dept. of Anaesthesiology,
DMCH, Ludhiana.

Co-Supervisor
Dr. Sandeep Kundra
Prof.,
Dept. of Anaesthesiology,
DMCH, Ludhiana.

Dr. Ashima Taneja
Prof. & Head,
Dept. of Obst. & Gyane.,

The student has to submit the three copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

S P Singh
Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

1. ***If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.***
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

COMPARISON OF INTRAVENOUS INFUSION OF LIGNOCAINE VERSUS DEXMEDETOMIDINE FOR POSTOPERATIVE PAIN RELIEF IN PATIENTS UNDERGOING TOTAL LAPAROSCOPIC HYSTERECTOMY

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

IN

ANAESTHESIA

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

NOVEMBER 2019

DR. VASUNDHARA JINDAL

DEPARTMENT OF ANAESTHESIA
DAYANAND MEDICAL COLLEGE AND HOSPITAL,
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	COMPARISON OF INTRAVENOUS INFUSION OF LIGNOCAINE VERSUS DEXMEDETOMIDINE FOR POSTOPERATIVE PAIN RELIEF IN PATIENTS UNDERGOING TOTAL LAPAROSCOPIC HYSTERECTOMY
For the degree of	M.D. Anaesthesia
Name of the candidate	Dr. Vasundhara Jindal
Supervisor	Dr. Dinesh Sood, Professor, Department of Anaesthesia, DMCH, Ludhiana
Co-supervisor	Dr. Sandeep Kundra, Professor, Department of Anaesthesia, DMCH, Ludhiana Dr. Ashima Taneja, Professor & Head, Department of Obstetrics & Gynaecology, DMCH, Ludhiana
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: A major concern after surgery is postoperative pain. Opioids, used for postoperative pain cause nausea and constipation. Epidural analgesia is not suitable for all patients. Thus, non-opioid local anaesthetic, lignocaine is being evaluated for its use in providing postoperative pain relief. Dexmedetomidine also has beneficial analgesic properties, thus can also reduce postoperative opioid consumption.

Aim of Study: To compare efficacy of perioperative I/v lignocaine and I/v dexmedetomidine on postoperative pain management after total laparoscopic hysterectomy.

Materials & methods: Sixty patients posted for total laparoscopic hysterectomy will be randomised into two groups. Group A patients will receive 1.5 mg/kg bolus dose of I/v lignocaine before induction, followed by 1 mg/kg/hr infusion, continued for 24 hours postoperatively. Group B patients will receive 1 µg/kg bolus dose of dexmedetomidine before induction followed by a 0.6 µg/kg/hr infusion, continued for 24 hours postoperatively. Postoperative pain and opioid consumption will be evaluated and studied in both the groups.

Clinical Significance: Whether I/v lignocaine and I/v dexmedetomidine can decrease the intensity of postoperative pain and decrease opioid consumption

Keywords: lignocaine, dexmedetomidine, pain postoperative, total laparoscopic hysterectomy

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"COMPARISON OF INTRAVENOUS INFUSION OF LIGNOCAINE VERSUS DEXMEDETOMIDINE FOR POSTOPERATIVE PAIN RELIEF IN PATIENTS UNDERGOING TOTAL LAPAROSCOPIC HYSTERECTOMY"** exist in the Department of Anaesthesia, DMC&H, Ludhiana and will be provided to be candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate herself under our supervision and guidance.

Supervisor

Dr. Dinesh Sood
Professor
Department of Anaesthesia
DMCH, Ludhiana

Co-Supervisor(s)

Dr. Sandeep Kundra
Professor
Department of Anaesthesia
DMCH, Ludhiana

Dr. Ashima Taneja
Professor & Head
Department of Obstetrics & Gynaecology
DMCH, Ludhiana

HEAD OF DEPARTMENT

Dr. Sunil Katyal
Professor and Head
Department of Anaesthesia
DMCH, Ludhiana

Place: LUDHIANA

Date: 7/12/19

APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Vasundhara Jindal
Department	Anaesthesia
Topic of Thesis	COMPARISON OF INTRAVENOUS INFUSION OF LIGNOCAINE VERSUS DEXMEDETOMIDINE FOR POSTOPERATIVE PAIN RELIEF IN PATIENTS UNDERGOING TOTAL LAPAROSCOPIC HYSTERECTOMY
Likely date of appearing in PG examination	MAY 2022
Date of enrollment	MAY 13, 2019
Name of Head of Department	Dr. Sunil Katyal
1) Supervisor **2) Co-Supervisor**	Dr. Dinesh Sood Dr. Sandeep Kundra Dr. Ashima Taneja
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Jaspal Singh (Professor & Head, Surgery)	Mr. A K Jindal (Member, Ethics Committee)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Assistant Dean Academics)	Dr. Deepinder K Chhina (Professor & Head, Microbiology)
Dr. Rajoo Singh Chhina (Dean Academics)	Dr. Neena Sood (Professor & Head, Pathology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / No

Dr. Sandeep Puri
Chairperson
Research Committee
Chairperson
Research Committee

Approved: Yes / No

Prof. Arvind Malhotra
Chairperson
Ethics Committee
Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	VASUNDHARA JINDAL SND HOSPITAL, BELA ROAD, RUPNAGAR, PUNJAB
2	NAME OF THE INSTITUTE	DAYANAND MEDICAL COLLEGE AND HOSPITAL, LUDHIANA
3	COURSE OF STUDY AND SUBJECT	DOCTOR OF MEDICINE IN ANAESTHESIOLOGY
4	DATE OF ADMISSION OF COURSE	13th MAY, 2019
5	TITLE OF THE TOPIC	COMPARISON OF INTRAVENOUS INFUSION OF LIGNOCAINE VERSUS DEXMEDETOMIDINE FOR POSTOPERATIVE PAIN RELIEF IN PATIENTS UNDERGOING TOTAL LAPAROSCOPIC HYSTERECTOMY

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Total laparoscopic hysterectomy (TLH) is a commonly performed gynecological procedure. Advantages of laparoscopic hysterectomy over traditional abdominal hysterectomy are- faster return to normal activities, lower intraoperative blood loss, shorter hospitalization, lesser infections and lesser postoperative pain. However, pain may still be quite severe, particularly in early postoperative period.[1]

Pain of TLH is- incisional pain, due to creation of pneumoperitoneum, stretching of intra-abdominal cavity, blood left in the abdomen, dissection of pelvic region. Also, laparoscopic surgeries are known to cause lesser pain so pain is often inadequately managed leading to higher incidence of post operative pain and higher opioid usage. Inadequate postoperative pain relief can result in basal atelactasis, pneumonia, deep vein thrombosis, pulmonary embolism, tachycardia, hypertension, myocardial ischemia and infarction. It also predisposes the patient to chronic pain, delayed wound healing and prolonged hospital stay, besides also leading to anxiety, sleep disorders, demoralization, disturbances in mental activity and social relations.[2] Pain within first three days must be timely detected and managed as this will facilitate early ambulation, mitigating the problems mentioned above.[3,4] Current postoperative analgesic regimens rely heavily on the use of systemic opioid analgesics. However, opioid analgesics are associated with adverse effects like nausea, vomiting, constipation, respiratory depression and opioid induced hyperalgesia. Thus, safer alternatives need to be evaluated.

Several techniques have been used for postoperative pain management like non steroidal anti-inflammatory drugs, dexamethasone, gabapentinoids, epidural analgesia, intraperitoneal instillation of local anaesthetics, and Transverse Abdominis Plane (TAP) block.[5] Dexamethasone exhibits dose dependant opioid sparing effect but doesn't decrease pain score. Gabapentin at higher doses has opioid sparing effect but is associated with side effects like dizziness, blurred vision. TAP block has no advantage in terms of

opioid consumption and no difference in pain score. Intraperitoneal local anaesthetic infusion has showed no analgesic effect in the setting of laparoscopic hysterectomy. Epidural analgesia is effective but is invasive so should be considered a reserve intervention. [1] One method of controlling postoperative pain is pre emptive analgesia i.e. prescribing analgesics before the stimulation of pain (before surgical incision) instead of when patient complains of pain. This provides a chance for analgesic drug to reach appropriate serum level and thus pain can be managed more effectively.[5]

Lignocaine is an amide local anaesthetic, that when injected intravenously, shows analgesic, antihyperalgesic and anti-inflammatory properties. It acts at the peripheral receptors, thus decreases the release of inflammatory mediators, and centrally modifies neuronal responses in spinal dorsal horn. These effects are mediated by a variety of mechanisms, like sodium channel blockade and inhibition of G-protein coupled receptors and N methyl D aspartate receptors.[7]

Dexmedetomidine is a selective alpha 2 adrenoceptor agonist with analgesic, sympatholytic and sedative properties, with minimal respiratory depression.[8] IV infusion of dexmedetomidine has been demonstrated to have significant post-operative opioid sparing effects, suggesting a role for this novel drug in multimodal analgesic techniques.[9] The proposed mechanism of action of dexmedetomidine includes blockade of C-neuronal activity and blockade of M3 receptors. Activation of alpha 2 adrenoceptors in brain and spinal cord inhibit neuronal firing, causing hypotension, bradycardia, sedation and analgesia.[10]

Thus, intravenous infusions of Lignocaine and Dexmedetomidine have both individually, been studied for relief of post-operative pain. However, very few studies have been conducted to compare IV infusion of these drugs. [11] The researchers in these studies administered IV infusion intra-operatively only and discontinued the infusion at the end of surgery. The potential analgesic effects of these drugs would be more, if the infusions are continued post-operatively as well.

Thus, the present study was planned to compare the effects of I/v infusion of lignocaine versus dexmedetomidine on postoperative pain relief and opioid consumption in patients undergoing total laparoscopic hysterectomy.

6.2 REVIEW OF LITERATURE

Total laparoscopic hysterectomy is being progressively used as an alternative to open abdominal hysterectomy for various gynaecological conditions because of advantages of reduced postoperative pain and morbidity, as well as earlier recovery and a shorter hospital stay. Nevertheless, one of the most important causes of postoperative morbidity and mortality is insufficiently treated pain.[2]

There are two types of pain - somatic pain and visceral pain. Somatic pain arises from activation of nociceptors of skin, muscle and soft tissue. Visceral pain results from activation of nociceptors of thoracic, pelvic or abdominal organs. Postoperative pain has both somatic and visceral components. Pain generated from laparoscopic hysterectomy includes incisional pain, which can be severe initially, but subsides within first half day, visceral pain, which takes longer (up to a day) to resolve and shoulder pain, which is milder, typically appears within 24 hours and can last for several days. Inadequate postoperative pain relief may not only delay recovery but also prolong hospital stay and increase medical costs.[1,12]

Perioperative pain cannot be effectively treated with a single medication. Therefore, it is recommended to use multimodal analgesia in perioperative period to eliminate over reliance on opioids for pain control and opioid related adverse effects. A combination to include opioids, non-steroidal anti-inflammatory drugs (NSAIDS) like acetaminophen, gabapentinoids, ketamine, dexmedetomidine and local anaesthetics administered by infiltration, regional block or intravenous route has been used.[13]

Mechanism of action of lidocaine in pain management suggests that it acts at the periphery and decreases the release of inflammatory mediators. It also centrally modifies the neuronal responses in the dorsal horn of spinal cord. Besides affecting the voltage gated sodium channels present in inflamed tissues, lidocaine affects the G- protein coupled receptors (GPCR), N methyl D aspartate(NMDA) receptors and potassium and calcium channels; thus interfering with conduction

of excitatory impulses on A-delta and C fibres, visceral pain, central sensitisation and immune responses.[11]

Analgesic mechanism of Dexmedetomidine is that dexmedetomidine is an alpha-2 adrenergic receptor agonist that directly targets the peripheral nervous system, causing a dose-dependant inhibition of C fibres and Ad fibres. Alpha-2 adrenergic receptors act on locus ceruleus area, inhibiting nociceptive transmission through the posterior horn of spinal cord. Alpha-2 adrenergic receptors also act on presynaptic membrane, inhibiting the release of norepinephrine which in turn induces hyperpolarization and inhibits pain signals to brain. Dexmedetomidine also promotes release of acetylcholine from spinal interneurons; the resulting increased synthesis and release of nitric oxide could be involved in regulation of analgesia.[14]

Various studies have shown the use of I/v lignocaine having analgesic effect. Lahiri S et al studied that intraoperative lignocaine infusion achieved earlier discharge criteria among laparoscopic cholecystectomy patients when lignocaine bolus 1.5mg/kg and 3mg/kg/hr infusion was given till extubation.[7] Lee U et al, in their study concluded that I/v lignocaine infusion given during bimaxillary surgery also reduces postoperative pain, analgesic consumption and facial swelling.[15] Kim KT conducted a study and concluded that VAS scores and fentanyl consumption was significantly lower in lignocaine group except after 48 hours after surgery, also lower incidence of postoperative nausea and vomiting was seen and decreased length of hospital stay in patients undergoing lumbar surgery.[16]
Tauzin-Fin P et al. demonstrated that I/v lignocaine infusion could reduce postoperative morphine consumption and improve postoperative pain management and postoperative rehabilitation after laparoscopic nephrectomy. [17] Page N, in her study concluded that I/v lignocaine infusion was effective for intractable pain in Ewing's sarcoma, where the pain score by Numerical rating scale(NRS) came down from 8/10 to 4/10 after first infusion. [16]

Gandhi KA et al studied that dexmedetomidine was also effective in providing analgesia without excessive sedation in patients undergoing cervical spine surgeries.[19] Analgesic properties of a dexmedetomidine infusion after uvulopalatopharyngoplasty in patients with obstructive sleep apnea were evaluated and Abdelmageed W. et al concluded that continuous dexmedetomidine infusion may be a useful analgesic adjuvant for patients susceptible to opioid induced respiratory depression.[9] Dexmedetomidine as an analgesic adjuvant during laparoscopic cholecystectomy was studied by Bielka K. et al and it was concluded that intraoperative DEX infusion reduced number of patients with severe postoperative pain, postoperative morphine consumption and prolong time to first use of rescue analgesia.[20] Habibi V et al studied the effect of dexmedetomidine on pain relief after cardiothoracic surgery and concluded that dexmedetomidine infusion provides safe, effective analgesia, decreases narcotic consumption and shows decreased trend of delirium without undesirable effect in cardiac surgery patients.[21] Kim D. et al studied the post operative analgesia effect of intravenous dexmedetomidine during ankle surgery under spinal anesthesia and concluded that intravenous dexmedetomidine reduced postoperative opioid consumption in first 24 hours.[22]

Aho M. et al studied the effect of i/v dexmedetomidine on pain after laparoscopic tubal ligation and found that it reduced opioid drug requirement but was attended by sedation and bradycardia.[23]

Shenghong Hu. Et al compared the effect of intravenous infusion of lidocaine and dexmedetomidine after thyroid surgery and concluded that both had equal effectiveness in providing analgesic effect after surgery.[24] Anis SG. Et al in their study concluded that lidocaine offered hemodynamic stability during pneumo-peritoneum, decreased the intensity of postoperative pain with opioid sparing, while offering a less sedated patient than dexmedetomidine during day case diagnostic laparoscopic gynaecological surgery.[25]

Side effects of lidocaine toxicity are dose dependant (at infusion >3 mg/min). At low plasma concentrations numbness of tongue and

perioral tissue is observed. At higher levels, vertigo, tinnitus, restlessness, speech difficulties, skeletal muscle twitching and drowsiness is reported. Dexmedetomidine causes analgesia without respiratory depression but its side effect is postoperative sedation.[8]

Extensive review of literature suggests that very few studies have been done to compare I/v lignocaine and I/v dexmedetomidine for postoperative pain relief. Hence, this study aims to compare the efficacy of I/v Lidocaine vs I/v Dexmedetomidine for postoperative pain relief in elective total laparoscopic hysterectomy cases.

6.3 AIMS AND OBJECTIVES

To compare efficacy of Intravenous infusion of lignocaine and dexmedetomidine in terms of:

1. Postoperative pain relief as assessed by visual analogue scale (VAS).
2. Postoperative opioid consumption.

7.0 MATERIALS AND METHODS

7.1 SOURCE OF DATA

The planned study will be conducted in the department of Anaesthesiology at Dayanand Medical College and Hospital, Ludhiana as a randomised double blinded study on a total of 60 patients to be taken for total laparoscopic hysterectomy under general anaesthesia after getting approved by the Ethics Committee of the Hospital.

7.2 METHOD OF COLLECTION OF DATA

PREANAESTHETIC CHECKUP

A thorough pre anaesthetic checkup including a detailed complete history and general physical and systemic examination will be performed a day prior to surgery. Baseline investigations like complete hemogram, serum electrolytes, coagulogram, random blood sugar, ECG, chest X-ray and other indicated investigations will be done before surgery. Patients will be educated about the study being conducted, visual analogue scale and that they can request for additional analgesic whenever they complain of pain and written informed consent will be taken.

Inclusion criteria -

Patients of age between 35-60 years belonging to ASA physical status I and II scheduled for elective total laparoscopic hysterectomy under general anaesthesia.

Exclusion criteria - Following patients will not be included in the study:

- Consent refusal.
- Patients on anti-arrythmic drugs.
- Patients with known history of coronary artery disease, liver disease.
- Allergic to a local anesthetic.
- Psychiatric patients.
- Inability to comprehend VAS.

Group allocations: Sixty patients will be randomly allocated into two groups- A and B of 30 patients each, according to computer generated

random numbers maintained in sequentially numbered, opaque envelopes.

Group A patients will receive IV infusion of lignocaine.

Group B patients will receive IV infusion of dexmedetomidine

A person not involved in the postoperative management of the patient will prepare the study drugs in a sterile syringe and administer the drugs to the patient. The candidate, blinded to the infusion of study drug, will record the postoperative vitals, VAS scores and pain relief data up to 24 hours following the surgical procedure.

PREMEDICATION

Prior to the surgery, patient will be kept fasting for a period of 8 hours. She will be given tablet Pantoprazole 40 mg and tablet Alprazolam 0.5mg on night before surgery with small sip of water.

ANAESTHESIA TECHNIQUE:

The study will be conducted on ASA I, II patients posted for total laparoscopic hysterectomy. After arrival of patient to the operating room, she will be positioned on the operating table in supine position and an intravenous (IV) line will be secured and IV fluids will be started. Routine monitoring including pulse oximetry, electrocardiography (ECG), non invasive blood pressure (NIBP), end tidal carbon dioxide ($EtCO_2$) will be done and baseline parameters will be noted.

Ten minutes before induction of anaesthesia, in group A patients, IV bolus of lignocaine 1.5mg/kg diluted to total volume of 20 ml with normal saline in a 50ml syringe, will be administered over a period of 10 minutes, followed by IV infusion of lignocaine 1mg/kg/hr diluted in normal saline, in a 50 ml syringe, through an infusion pump, during entire surgical procedure and for first 24 hours after surgery. Group B patients will receive IV bolus of 1 microgram/kg of dexmedetomidine diluted to a total volume of 20 ml with normal saline, in a 50 ml syringe, 10 minutes before the induction of anaesthesia, over a period of 10 minutes, and subsequently an infusion of 0.6 microgram/kg/hr diluted in normal saline, in a 50 ml syringe, throughout surgery and for first 24 hours after surgery.

Patients will be administered injection (Inj) metoclopramide 10mg IV, Inj. fentanyl 2 microgram/kg IV, and Inj. Glycopyrrolate 0.2mg IV. All patients will be pre oxygenated with 100% oxygen for 3 minutes. For anaesthesia induction, Inj. Propofol 1.5-2 mg/kg IV will be injected slowly till there is loss of verbal response. Loading dose of atracurium 0.5mg/kg IV will be given. Direct laryngoscopy will be performed three minutes later and trachea will be intubated with an appropriate sized cuffed endotracheal tube. Cuff will be inflated and placement of tube in trachea will be confirmed by bilateral equal air entry on chest auscultation and end tidal CO_2. The patients will be mechanically ventilated with ventilator using volume controlled mode of ventilation. Desflurane will be used to maintain anaesthesia titrated according to the hemodynamic parameters of the patient.

The entire surgical procedure done in the study will be performed by a single surgeon thus limiting surgical variation.

During the surgery, doses of inj. atracurium 0.1 mg/kg will be given for the maintenance of relaxation, while monitoring the heart rate, blood pressure, respiratory rate, SpO_2. Injection fentanyl 0.5 microgram/kg will be given after every 1 hour.

Inj. Diclofenac sodium 75 mg I/v first dose, in 100 ml normal saline, will be given 30 minutes before expected extubation and then every 8 hourly as a part of the multimodal analgesia regimen. At the end of surgery, Inj. Ondansetron 0.1mg/kg IV will be given. After closure of the skin all anaesthetic agents will be stopped.

Trachea will be extubated after administering Inj. Neostigmine 0.05mg/kg IV and Inj. Glycopyrrolate 0.01 mg/kg IV, at the discretion of the attending anaesthesiologist and when respiratory efforts of patient become regular and patient becomes responsive.

Patients will be transferred to post anaesthesia care unit (PACU) and this time will be labelled as zero. In PACU, the infusion of the study drug will be continued for 24 hours postoperatively. Patients will also receive Inj. Diclofenac sodium 75 mg IV 8 hourly in postoperative period.

During the first 24 hours in PACU, postoperative pain will be assessed using Visual Analogue Scale (0-10). [Fig-1][26]

Visual analogue scale having 0 to 10 equidistant markings will be shown and explained to patient. Pain scoring will be done by asking the patient to choose along the scale with 0 corresponding to 'no pain' and 10 corresponding to ' worst imaginable pain'. The intensity of pain felt by patient will be scored at fixed intervals after surgery.

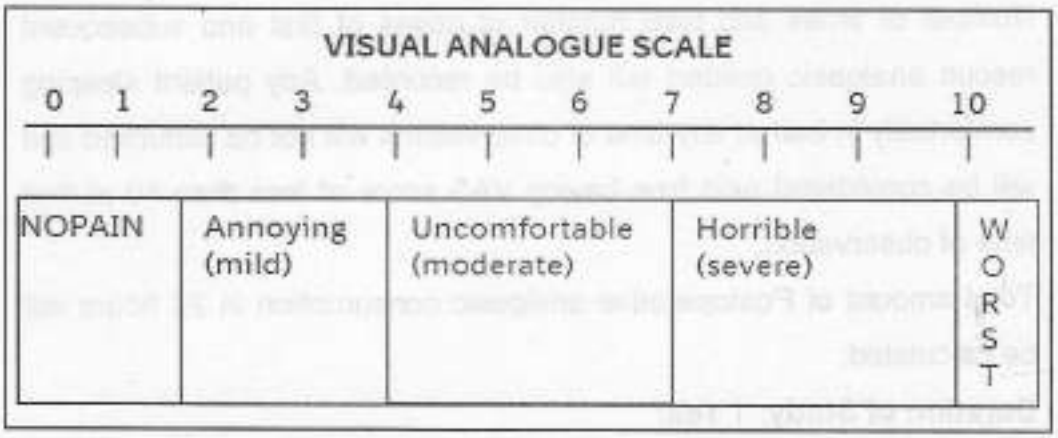

Fig-1[26]

Whenever the patient will complain of pain post operatively, a rescue analgesic - Tramadol 50mg I/v in 100 ml normal saline will be administered, to maintain a VAS of ≤ 3 at rest. Dose and time of first rescue analgesic will be noted. If patient still complains of pain even after 15 minutes of receiving tramadol, same doses will be repeated up to a maximum of 100 mg in contiguous 4 hours or 400 mg in 24 hours. If patient still complains of pain, then fentanyl 1mcg/kg bolus dose will be given as second rescue analgesic.

Bradycardia defined as heart rate less than 60 beats/min, will be treated with IV atropine sulphate 0.01mg/kg.[27] Hypotension will be defined as decrease of systolic blood pressure to < 80% of the baseline value or combination of two criteria i.e. systolic blood pressure < 100mmHg or a decrease to <80 % of the baseline.[28] It will be treated by IV boluses of 100 ml of crystalloid fluids and ephedrine 6mg IV as required.

Sedation will be assessed using Ramsay Sedation Score.[29]

1= patient is anxious and agitated or restless, or both

2= patient is cooperative, oriented and tranquil

3= patient responds to commands only

4= patient exhibits brisk response to light glabellar tap or loud auditory stimulus

5= patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus

6= patient exhibits no response

Number of times and total number of doses of first and subsequent rescue analgesic needed will also be recorded. Any patient sleeping comfortably in bed at any time of observations will not be disturbed and will be considered pain free having VAS score of less than 40 at that time of observation.

Total amount of Postoperative analgesic consumption in 24 hours will be calculated.

Duration of Study: 1 Year

OUTCOME: The outcome of the study will be evaluated in terms of

PRIMARY OUTCOME measures:

1. Post-operative VAS score
2. Total opioid consumption in 24 hours

SECONDARY OUTCOME measures:

1. Time of administration of first and subsequent rescue analgesic and number of times rescue analgesic needs to be given.
2. The adverse effects of the drugs such as nausea, vomiting, hypotension, sedation, bradycardia.

Statistical analysis: Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups will be done using Student t-test and Mann Whitney U test for independent samples for parametric and non-parametric data respectively. For comparing categorical data, Chi square ($\chi 2$) test will be performed and exact test was used when the expected frequency is less than 5. A probability

value (p value) less than 0.05 will be considered statistically significant. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Complete hemogram, serum electrolytes, coagulogram, random blood sugar, ECG, chest X-ray.

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Yes, attached herewith.

8. LIST OF REFERENCES

1. Lirk P, Thiry J, Bonnet MP, Joshi GP, Bonnet F. Pain management after laparoscopic hysterectomy: systematic review of literature and prospect recommendations. Regional Anesthesia & Pain Medicine. 2019;44:425-36.
2. Beyaz SG, Bayar F, Erdem AF. Acute Postoperative pain. J Anesthe Clinic Res. 2011;4:286.
3. Choi JB, Kang K, Song MK, Seok S, Kim YH, Kim JE. Pain Characteristics after Total Laparoscopic Hysterectomy. Int J Med Sci. 2016;13:562-8.
4. McCartney CJL, McLoed GA. Local Infiltration Analgesia for total knee arthroplasty. Br J Anaesth. 2011;107:487-9.
5. Garimella V, Cellini C. Postoperative pain control. Clin Colon Rectal Surg. 2013;26:191-6.
6. Farzi F, Nabi BN, Mirmansouri A, Fakoor F, Roshan ZA, Biazar G, et al. Postoperative pain after abdominal hysterectomy: a randomized, double-blind, controlled trial comparing the effects of tramadol and gabapentin as premedication. Anesth Pain Med. 2016;6:e32360.
7. Lahiri S, Das S, Basu SR. Intraoperative lignocaine infusion achieving earlier discharge criteria among laparoscopic cholecystectomy patients. Saudi J Laparosc. 2018;3:16-20.
8. Li SY, Li H, Ni J, Ma YS. Comparison of intravenous lidocaine and dexmedetomidine infusion for prevention of postoperative catheter-related bladder discomfort: a randomized controlled trial. BMC anesthesiology. 2019;19:37.
9. Abdelmageed WM, Elquesny KM, Shabana RI, Abushama HM, Nassar AM. Analgesic properties of a dexmedetomidine infusion after uvulopalatopharyngoplasty in patients with obstructive sleep apnea. Saudi J Anaesth. 2011;5:150-6.
10. Cassuto J, Sinclair R, Bonderovic M. Anti-inflammatory properties of local anesthetics and their present and potential clinical implications. Acta Anaesthesiol Scand. 2006;50:265-82.

11. Menshawi MA, Fahim HM. Dexmedetomidine versus lidocaine as an adjuvant to general anesthesia for elective abdominal gynecological surgeries. Ain-Shams Journal of Anesthesiology. 2019;11:12.
12. Kehlet H, Holte K. Effect of postoperative analgesia on surgical outcome. Br J Anaesth 2001;87:62-72.
13. Schwenk ES, Mariana ER. Designing the ideal perioperative pain management plan starts with multimodal analgesia. Korean J Anesthesiol. 2018;71:345-52.
14. Tang C, Xia Z. Dexmedetomidine in perioperative acute pain management: a non- opioid adjuvant analgesic. J Pain Res. 2017;10:1899-904.
15. Lee U, Choi YJ, Choi GJ, Kang H. Intravenous lidocaine for effective pain relief after bimaxillary surgery. Clin Oral Investig. 2017;21:2645-52.
16. Kim KT, Cho DC, Sung JK. Intraoperative systemic infusion of lidocaine reduces postoperative pain after lumbar surgery. Spine J. 2014;14:1559-66.
17. Tauzin-Fin P, Bernard O, Sesay M. Benefits of intravenous lidocaine on post-operative pain and acute rehabilitation after laparoscopic nephrectomy. J Anaesthesiol Clin Pharmacol. 2014;30:366-72.
18. Page N. Intravenous lignocaine infusion for intractable pain in Ewing's Sarcoma. Indian J Palliat Care. 2018;24:115-6.
19. Gandhi KA, Panda NB, Vellaichamy A, Matthew PJ, Sahni N, Batra YK. Intraoperative and Postoperative Administration of dexmedetomidine reduces anesthetic and postoperative analgesic requirements in patients undergoing cervical spine injuries. J Neurosurg Anaesthesiol. 2017;29:258-63.
20. Bielka K, Kuchyn I, Babych V, Martycshenko K, Inozemtsev O. Dexmedetomidine infusion as an analgesic adjuvant during laparoscopic cholecystectomy: a randomized controlled study. BMC anesthesiology. 2018;18:44.

PROFORMA

MRD No. S. No.

Admission no. DOA

Age/Sex

PRE ANAESTHETIC CHECKUP:

History of Patient illness :-

History of past illness :-

History of previous surgery :-

History of drug intake/ allergy :-

GENERAL PHYSICAL EXAMINATION:

Height	Weight	BMI
Pallor	Clubbing	Cyanosis
JVP	Edema	Jaundice
Lymphadenopathy	Trachea	Thyroid
Pulse rate	Respiratory rate	BP
Temperature	BHT	Mouth opening
TM joint mobility	Teeth	Spine
Mallampatti Grade I II III IV		ASA Grade

Signature of Candidate **Signature of Supervisor**

SYSTEMIC EXAMINATION:

Central nervous system:

Respiratory System:

Cardiovascular System:

Abdominal examination:

INVESTIGATIONS:

Hemoglobin/ TLC/ Platelet count/ PCV:

BT/CT:

Surgery start time **Anaesthesia start time**

Surgery finish time **Anaesthesia finish time**

	SBP	DBP	HR	SPO_2	VAS	Drug, Dose and Time of 1st dose of rescue analgesic	Drug, Dose and Time of 2nd dose of rescue analgesic	Drug, Dose ar Time of subsequent d of rescue analgesic
Immediately in PACU (zero hour)								
1 hour								
2 hours								
3 hours								
4 hours								
5 hours								
6 hours								
8 hours								
10 hours								
12 hours								
16 hours								
20 hours								
24 hours								

Signature of Candidate **Signature of Supervisor**

Time of 1st dose of rescue analgesic given:

Time of 2nd dose of rescue analgesic given:

Time of subsequent rescue analgesics given in 24 hrs:

Number of times rescue analgesic needed:

Total opioid consumption in 24 hours:

Total analgesic consumption in 24 hours:

Adverse effects if any such as hypotension, headache, bradycardia

Assessment of sedation will be done according to Ramsay Sedation Score

	Sedation score	Dose and time of i/v atropine	Dose and time of i/v ephedrine
Immediately in PACU(ZERO HOUR)			
1 hour			
2 hours			
3 hours			
4 hours			
5hours			
6 hours			
8 hours			
10 hours			
12 hours			
16 hours			
20 hours			
24 hours			

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o,

S/o..... .....am willing to participate in the study **"COMPARISON OF INTRAVENOUS INFUSION OF LIGNOCAINE VERSUS DEXMEDETOMIDINE FOR POSTOPERATIVE PAIN RELIEF IN PATIENTS UNDERGOING TOTAL LAPAROSCOPIC HYSTERECTOMY"**

The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

....

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य "COMPARISON OF INTRAVENOUS INFUSION OF LIGNOCAINE VERSUS DEXMEDETOMIDINE FOR POSTOPERATIVE PAIN RELIEF IN PATIENTS UNDERGOING TOTAL LAPAROSCOPIC HYSTERECTOMY" में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫ਼ਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"COMPARISON OF INTRAVENOUS INFUSION OF LIGNOCAINE VERSUS DEXMEDETOMIDINE FOR POSTOPERATIVE PAIN RELIEF IN PATIENTS UNDERGOING TOTAL LAPAROSCOPIC HYSTERECTOMY" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ